

Toxicology Research Laboratory

UIC The University of Illinois
at Chicago

Department of Pharmacology (M/C 868)
1940 W. Taylor St.
Chicago, Illinois 60612-7353

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Contract No.: DAMD17-92-C-2001
Task Order No.: UIC-18A
UIC/TRL Study No.: 193

Title Page

Volume 2 of 2

Study Report for Task Order No. UIC-18A
THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

Sponsor: US Army Medical Materiel
Development Activity

Test Article: WR242511 Tartrate

Contract No.: DAMD17-92-C-2001

Study Director

Barry S. Levine, D.Sc., D.A.B.T.

In-Life Phase Completed On

March 07, 1996

Performing Laboratory

TOXICOLOGY RESEARCH LABORATORY (TRL)
University of Illinois at Chicago (UIC)
Department of Pharmacology
1940 W. Taylor St.
Chicago, IL 60612-7353

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Contract No.: DAMD17-92-C-2001
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APPENDIX G
Individual Hematology Data

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

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Hematology Test Directory

STUDY: UIC-18

NO.	ABBR. UNITS	DESCRIPTION PRECISION	CALCULATED	OPERAND A	OPERAND B	---LOWER LIMIT---		---UPPER LIMIT---	
						MALE	FEMALE	MALE	FEMALE
1.	RBC 10 ⁶ /mm ³	Erythrocytes 0.00	NO			6.00	6.00	8.00	8.00
2.	HGB g/dL	Hemoglobin 0.0	NO			14.0	14.0	19.0	19.0
3.	HCT %	Hematocrit 0.0	NO			41.0	41.0	55.0	55.0
4.	MCV fL	Mean Corpuscular Volume 0.0	NO			65.0	65.0	73.0	73.0
5.	MCH pg	Mean Corpuscular Hemo. 0.0	NO			22.0	22.0	26.0	26.0
6.	MCHC g/dL	Mean Corpus. Hemo. Conc. 0.0	NO			33.0	33.0	37.0	37.0
7.	RETICS % RBCs	Reticulocytes 0.0	NO			0.0	0.0	0.8	0.8
8.	HEINZ BOD. % RBCs	Heinz Bodies 0.0	NO			0.0	0.0	0.5	0.5
9.	% METHGB % HGBs	% Methemoglobin 0.0	NO			0.0	0.0	2.5	2.5
10.	PLT 10 ³ /mm ³	Platelets Integer	NO			200	200	500	500
11.	PT sec	Prothrombin Time 0.0	NO			6.0	6.0	9.0	9.0
12.	APTT sec	Act. Partial Thrombo. Time 0.0	NO			9.0	9.0	13.0	13.0
13.	WBC 10 ³ /mm ³	Leukocytes 0.0	NO			6.0	6.0	15.0	15.0

(END OF REPORT)

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

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193 MORPHOLOGY DICTIONARY

ABBR	DESCRIPTION
1. AN	Anisocytosis
2. HC	Hypochromia
3. NR	Nucleated Red Blood Cells
4. PC	Polychromasia
5. BS	Basophilic Stippling
6. MI	Microcytes
7. OV	Ovalocytes
8. SK	Sickle Cells
9. HB	Heinz Bodies
10. MA	Macrocytes
11. PK	Poikilocytes
12. SP	Spherocytes
13. HJ	Howell-Jolly Bodies
14. NN	Normocytic & Normochromic
15. TG	Target Cells
16. LP	Large Platelets
17. CP	Clumped Platelets
18. RF	Rouleaux Formation
19. NRC	Normal Red Blood Cells
20. TX	Toxic Granule
21. PY	Pyknotic Cells
22. RL	Reactive Lymphocytes
23. VA	Vacuoles

193 DETAIL DICTIONARY

ABBR	DESCRIPTION
1. 1	Slight
2. 2	Moderate
3. 3	Mod. to Marked
4. 4	Marked

(END OF REPORT)

HISTORICAL DATABASE REPORT

		% METHGB	APTT	FIBRIN	HB	HCT	HGB	MCH	MCHC
DOG BEAGLE Male									
CONTROL DATA	MEAN	1.1	11.0	186	0.1	44.3	15.4	24.2	34.7
	SD	0.75	0.96	51.3	0.09	2.88	1.01	0.69	0.62
	N	99	129	28	36	133	133	133	133
DOG BEAGLE Female									
CONTROL DATA	MEAN	0.9	11.0	162	0.1	45.9	16.1	24.8	35.0
	SD	0.53	1.11	34.2	0.11	3.18	1.10	0.58	0.66
	N	100	128	28	36	129	129	129	129
DOG BEAGLE Both									
CONTROL DATA	MEAN	1.0	11.0	174	0.1	45.1	15.7	24.5	34.9
	SD	0.66	1.03	44.8	0.10	3.13	1.11	0.72	0.66
	N	199	257	56	72	262	262	262	262

CONTROL DATA-189-336 days

LABCAT CC4.32

UIC/TRL - HEMATOLOGY

HISTORICAL DATABASE REPORT

		MCV	PLT	PT	RBC	RETICS	WBC
DOG BEAGLE Male							
CONTROL DATA	MEAN	69.6	286	7.8	6.37	0.4	8.2
	SD	1.58	72.4	0.71	0.428	0.27	1.88
	N	133	133	129	133	131	133
DOG BEAGLE Female							
CONTROL DATA	MEAN	70.8	292	7.8	6.48	0.4	8.7
	SD	1.78	74.8	0.70	0.446	0.27	1.75
	N	129	129	128	129	123	129
DOG BEAGLE Both							
CONTROL DATA	MEAN	70.2	289	7.8	6.42	0.4	8.5
	SD	1.80	73.5	0.70	0.440	0.27	1.83
	N	262	262	257	262	254	262

CONTROL DATA-189-336 days

LABCAT CC4.32

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Erythrocytes

STUDY ID: UIC-18
STUDY NO: 193
ABBR: RBC

SEX: MALE

UNITS: $10^6/\text{mm}^3$

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
-----------	---------	---------	--------	--------	---------	---------	---------

GROUP: 1-M:0 mg base/kg/day

8656	7.44	6.68	6.61	6.84	6.66	--	--
8687	7.44	6.58	6.84	6.69	6.68	--	--
8669	6.23	5.83	5.94	7.18	6.78	--	--
8673	7.14	6.75	6.80	6.98	6.91	--	--
8667	6.87	6.21	6.77	7.15	6.91	7.00	6.65
8654	6.49	6.28	5.90	6.77	6.28	6.33	6.66
8680	6.65	6.92	6.35	6.80	6.54	6.33	7.36
8676	6.54	6.72	6.70	6.92	6.22	7.25	7.16

MEAN	6.85	6.50	6.49	6.92	6.62	6.73	6.96
SD	0.452	0.360	0.383	0.177	0.262	0.470	0.359
N	8	8	8	8	8	4	4

GROUP: 2-M:0.1 mg base/kg/day

8685	6.36	6.70	7.30	6.86	6.90	--	--
8663	6.50	6.29	6.21	6.78	6.14	--	--
8686	6.30	6.30	6.21	6.29	6.61	--	--
8665	6.77	6.66	6.44	6.30	6.92	6.69	6.76
8666	6.69	6.42	6.88	6.83	6.36	7.11	7.19
8655	7.05	6.28	6.11	7.06	6.88	6.58	7.13
8659	7.00	6.41	6.94	7.34	7.34	7.32	6.98
8677	6.33	6.94	7.43	6.82	7.20	--	--

MEAN	6.63	6.50	6.69	6.79	6.79	6.93	7.02
SD	0.299	0.241	0.518	0.353	0.405	0.349	0.192
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Erythrocytes

STUDY ID: UIC-18
STUDY NO: 193
ABBR: RBC

SEX: MALE

UNITS: $10^6/\text{mm}^3$

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
GROUP: 3-M:0.3 mg base/kg/day							
8674	6.58	6.19	5.88	6.00	5.90	6.28	6.47
8653	7.22	6.54	6.98	5.65	6.49	--	--
8660	6.29	5.93	6.13	6.79	6.54	--	--
8668	7.06	6.28	6.15	6.40	6.28	--	--
8682	5.77	6.43	5.76	5.45	5.31	5.99	6.33
8684	6.71	6.80	6.49	6.52	7.40	--	--
8662	7.14	6.06	6.69	6.33	6.56	6.55	7.26
8688	7.02	6.43	7.27	7.27	7.57	8.47	8.09
MEAN	6.72	6.33	6.42	6.30	6.51	6.82	7.04
SD	0.498	0.278	0.534	0.595	0.735	1.122	0.812
N	8	8	8	8	8	4	4

GROUP: 4-M:1.0 mg base/kg/day							
8661	7.66	7.27	6.86	7.22	6.77	--	--
8670	5.73	6.33	5.55	7.00	6.72	--	--
8681	6.64	6.70	5.29	7.07	6.34	--	--
8664	6.06	6.11	5.45	6.06	6.47	--	--
8675	5.92	5.72	5.78	6.66	5.91	6.94	6.20
8683	6.68	6.71	5.81	6.87	6.30	7.36	7.71
8658	6.25	6.54	6.08	6.64	5.92	6.50	6.79
8652	6.58	6.42	6.32	6.66	7.32	6.85	7.08
MEAN	6.44	6.48	5.89	6.77	6.47	6.91	6.95
SD	0.605	0.458	0.514	0.359	0.469	0.354	0.628
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Hemoglobin

STUDY ID: UIC-18
STUDY NO: 193
ABBR: HGB

SEX: MALE

UNITS: g/dL

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
-----------	---------	---------	--------	--------	---------	---------	---------

GROUP: 1-M:0 mg base/kg/day

8656	17.9	16.0	15.9	16.7	16.1	--	--
8687	17.6	15.6	16.1	16.2	16.3	--	--
8669	15.5	14.4	14.5	17.4	16.9	--	--
8673	16.5	16.1	15.7	16.5	16.2	--	--
8667	17.1	15.4	16.8	17.7	17.8	17.3	15.9
8654	15.5	15.3	14.5	16.4	15.4	14.9	15.8
8680	16.3	17.0	15.5	16.6	16.3	15.7	17.5
8676	15.4	15.9	15.6	16.4	14.8	17.1	16.9

MEAN	16.5	15.7	15.6	16.7	16.2	16.3	16.5
SD	0.98	0.75	0.78	0.53	0.90	1.15	0.82
N	8	8	8	8	8	4	4

GROUP: 2-M:0.1 mg base/kg/day

8685	14.5	15.0	16.3	15.6	16.1	--	--
8663	16.0	15.4	14.8	16.7	15.2	--	--
8686	15.0	15.1	14.6	14.7	15.6	--	--
8665	16.2	16.0	15.0	15.0	16.5	15.4	15.9
8666	16.3	15.2	16.3	16.6	15.6	16.9	16.9
8655	17.4	15.6	14.9	17.5	17.3	16.2	17.5
8659	17.3	16.1	17.1	18.4	18.3	18.0	17.1
8677	15.4	17.2	18.3	16.6	18.1	--	--

MEAN	16.0	15.7	15.9	16.4	16.6	16.6	16.9
SD	1.03	0.73	1.32	1.25	1.19	1.10	0.68
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Hemoglobin

STUDY ID: UIC-18
STUDY NO: 193
ABBR: HGB

SEX: MALE

UNITS: g/dL

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
GROUP: 3-M:0.3 mg base/kg/day							
8674	15.4	14.7	14.3	14.3	14.1	14.4	15.3
8653	17.7	16.1	17.0	14.0	16.0	--	--
8660	14.9	14.2	14.9	16.3	15.6	--	--
8668	17.4	15.4	15.5	15.8	15.5	--	--
8682	14.4	15.8	14.2	14.2	13.0	14.2	15.0
8684	16.2	16.2	15.7	15.8	17.9	--	--
8662	17.5	14.9	16.2	15.4	15.8	15.0	16.7
8688	16.0	15.1	16.9	16.8	17.8	19.2	18.7
MEAN	16.2	15.3	15.6	15.3	15.7	15.7	16.4
SD	1.25	0.71	1.08	1.05	1.66	2.36	1.69
N	8	8	8	8	8	4	4

GROUP: 4-M:1.0 mg base/kg/day							
8661	17.6	16.6	16.1	16.9	15.9	--	--
8670	14.4	15.7	14.0	17.3	16.8	--	--
8681	15.7	15.7	13.1	16.8	15.3	--	--
8664	15.4	15.3	13.7	15.0	15.7	--	--
8675	14.9	14.7	14.9	16.6	15.1	16.7	15.1
8683	16.3	16.4	14.4	16.6	15.5	17.8	18.5
8658	15.5	16.1	15.7	16.8	15.0	16.0	16.4
8652	16.5	16.0	15.6	16.8	18.3	16.8	17.0
MEAN	15.8	15.8	14.7	16.6	16.0	16.8	16.8
SD	1.00	0.61	1.07	0.68	1.11	0.74	1.41
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Hematocrit

STUDY ID: UIC-18

SEX: MALE

STUDY NO: 193

ABBR: HCT

UNITS: %

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
-----------	---------	---------	--------	--------	---------	---------	---------

GROUP: 1-M:0 mg base/kg/day

8656	52.3	46.8	46.5	48.2	47.3	--	--
8687	51.5	45.4	47.5	46.0	46.4	--	--
8669	44.7	42.0	41.6	50.6	47.9	--	--
8673	48.1	45.8	46.0	46.8	46.1	--	--
8667	49.1	44.2	48.3	50.8	49.5	50.3	47.7
8654	44.7	43.2	40.9	46.6	43.5	42.9	44.9
8680	47.6	49.4	45.1	47.9	47.1	45.5	52.1
8676	44.3	45.8	45.4	46.7	42.5	49.2	48.6

MEAN	47.8	45.3	45.2	48.0	46.3	47.0	48.3
SD	3.10	2.27	2.64	1.84	2.29	3.41	2.97
N	8	8	8	8	8	4	4

GROUP: 2-M:0.1 mg base/kg/day

8685	41.6	43.3	47.6	45.0	46.0	--	--
8663	45.1	43.7	43.2	46.4	42.8	--	--
8686	42.9	42.6	41.0	41.3	43.8	--	--
8665	45.6	44.7	43.4	42.4	46.5	44.6	45.4
8666	45.8	43.8	47.1	46.4	44.0	48.0	48.7
8655	49.4	44.0	42.6	56.3	48.6	45.8	49.9
8659	50.1	45.4	49.4	59.4	52.6	52.0	49.6
8677	45.2	50.2	52.7	47.9	51.3	--	--

MEAN	45.7	44.7	45.9	48.1	47.0	47.6	48.4
SD	2.89	2.37	3.99	6.43	3.60	3.25	2.06
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Hematocrit

STUDY ID: UIC-18
STUDY NO: 193
ABBR: HCT

SEX: MALE

UNITS: %

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
-----------	---------	---------	--------	--------	---------	---------	---------

GROUP: 3-M:0.3 mg base/kg/day

8674	44.5	41.6	40.2	40.4	39.4	41.7	43.3
8653	50.3	45.9	50.1	40.6	44.5	--	--
8660	43.3	40.6	42.5	46.9	44.9	--	--
8668	51.3	45.3	45.1	46.3	45.4	--	--
8682	42.2	47.5	42.7	45.8	38.4	41.9	44.0
8684	46.6	47.5	45.9	46.5	52.0	--	--
8662	50.5	42.6	47.0	44.0	44.6	43.9	48.0
8688	46.4	43.0	48.9	48.9	50.5	55.9	53.8

MEAN	46.9	44.3	45.3	44.9	45.0	45.9	47.3
SD	3.49	2.66	3.38	3.04	4.70	6.77	4.82
N	8	8	8	8	8	4	4

GROUP: 4-M:1.0 mg base/kg/day

8661	51.2	48.5	47.5	49.1	45.0	--	--
8670	40.9	45.4	41.6	50.4	48.5	--	--
8681	45.9	46.4	39.0	49.8	44.3	--	--
8664	43.8	44.4	40.2	46.0	45.4	--	--
8675	43.4	42.4	44.6	48.6	43.3	50.5	44.0
8683	47.5	47.5	43.0	49.3	45.5	52.6	53.1
8658	45.3	47.3	45.8	48.3	42.7	46.9	48.1
8652	47.1	46.0	46.3	48.8	53.1	49.3	49.5

MEAN	45.6	46.0	43.5	48.8	46.0	49.8	48.7
SD	3.11	1.94	3.06	1.31	3.37	2.38	3.76
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Mean Corpuscular Volume

STUDY ID: UIC-18
STUDY NO: 193
ABBR: MCV

SEX: MALE

UNITS: fL

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
-----------	---------	---------	--------	--------	---------	---------	---------

GROUP: 1-M:0 mg base/kg/day

8656	70.3	70.1	70.3	70.5	71.0	--	--
8687	69.2	69.0	69.4	68.8	69.5	--	--
8669	71.7	72.0	70.0	70.5	70.6	--	--
8673	67.4	67.9	67.6	67.0	66.7	--	--
8667	71.5	71.2	71.3	71.0	71.6	71.9	71.7
8654	68.9	68.8	69.3	68.8	69.3	67.8	67.4
8680	71.6	71.4	71.0	70.4	72.0	71.9	70.8
8676	67.7	68.2	67.8	67.5	68.3	67.9	67.9

MEAN	69.8	69.8	69.6	69.3	69.9	69.9	69.5
SD	1.75	1.57	1.36	1.51	1.79	2.34	2.12
N	8	8	8	8	8	4	4

GROUP: 2-M:0.1 mg base/kg/day

8685	65.4	64.6	65.2	65.6	66.7	--	--
8663	69.4	69.5	69.6	68.4	69.7	--	--
8686	68.1	67.6	66.0	65.7	66.3	--	--
8665	67.4	67.1	67.4	67.3	67.2	66.7	67.2
8666	68.5	68.2	68.5	67.9	69.2	67.5	67.7
8655	70.1	70.1	69.7	79.7	70.6	69.6	70.0
8659	71.6	70.8	71.2	80.9	71.7	71.0	71.1
8677	71.4	72.3	70.9	70.2	71.3	--	--

MEAN	69.0	68.8	68.6	70.7	69.1	68.7	69.0
SD	2.09	2.41	2.20	6.11	2.12	1.96	1.86
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Mean Corpuscular Volume

STUDY ID: UIC-18
STUDY NO: 193
ABBR: MCV

SEX: MALE

UNITS: fL

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
GROUP: 3-M:0.3 mg base/kg/day							
8674	67.6	67.2	68.4	67.3	66.8	66.4	66.9
8653	69.7	70.2	71.8	71.9	68.6	--	--
8660	68.8	68.5	69.3	69.1	68.7	--	--
8668	72.7	72.1	73.3	72.3	72.3	--	--
8682	73.1	73.9	74.1	84.0	72.3	69.9	69.5
8684	69.4	69.9	70.7	71.3	70.3	--	--
8662	70.7	70.3	70.3	69.5	68.0	67.0	66.1
8688	66.1	66.9	67.3	67.3	66.7	66.0	66.5
MEAN	69.8	69.9	70.7	71.6	69.2	67.3	67.3
SD	2.38	2.37	2.34	5.37	2.22	1.77	1.54
N	8	8	8	8	8	4	4

GROUP: 4-M:1.0 mg base/kg/day							
8661	66.8	66.7	69.2	68.0	66.5	--	--
8670	71.4	71.7	75.0	72.0	72.2	--	--
8681	69.1	69.3	73.7	70.4	69.9	--	--
8664	72.3	72.7	73.8	75.9	70.2	--	--
8675	73.3	74.1	77.2	73.0	73.3	72.8	71.0
8683	71.1	70.8	74.0	71.8	72.2	71.5	68.9
8658	72.5	72.3	75.3	72.7	72.1	72.2	70.8
8652	71.6	71.7	73.3	73.3	72.5	72.0	69.9
MEAN	71.0	71.2	73.9	72.1	71.1	72.1	70.2
SD	2.10	2.28	2.29	2.29	2.19	0.54	0.96
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Mean Corpuscular Hemo.

STUDY ID: UIC-18
STUDY NO: 193
ABBR: MCH

SEX: MALE

UNITS: pg

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
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GROUP: 3-M:0.3 mg base/kg/day

8674	23.4	23.7	24.3	23.8	23.9	22.9	23.6
8653	24.5	24.6	24.4	24.8	24.7	--	--
8660	23.7	23.9	24.3	24.0	23.9	--	--
8668	24.6	24.5	25.2	24.7	24.7	--	--
8682	25.0	24.6	24.7	26.1	24.5	23.7	23.7
8684	24.1	23.8	24.2	24.2	24.2	--	--
8662	24.5	24.6	24.2	24.3	24.1	22.9	23.0
8688	22.8	23.5	23.2	23.1	23.5	22.7	23.1

MEAN	24.1	24.2	24.3	24.4	24.2	23.1	23.4
SD	0.73	0.47	0.56	0.88	0.43	0.44	0.35
N	8	8	8	8	8	4	4

GROUP: 4-M:1.0 mg base/kg/day

8661	23.0	22.8	23.5	23.4	23.5	--	--
8670	25.1	24.8	25.2	24.7	25.0	--	--
8681	23.6	23.4	24.8	23.8	24.1	--	--
8664	25.4	25.0	25.1	24.8	24.3	--	--
8675	25.2	25.7	25.8	24.9	25.5	24.1	24.4
8683	24.4	24.4	24.8	24.2	24.6	24.2	24.0
8658	24.8	24.6	25.8	25.3	25.3	24.6	24.2
8652	25.1	24.9	24.7	25.2	25.0	24.5	24.0

MEAN	24.6	24.5	25.0	24.5	24.7	24.4	24.2
SD	0.86	0.93	0.73	0.68	0.67	0.24	0.19
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Mean Corpus. Hemo. Conc.

STUDY ID: UIC-18
STUDY NO: 193
ABBR: MCHC

SEX: MALE

UNITS: g/dL

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
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GROUP: 1-M:0 mg base/kg/day

8656	34.2	34.2	34.2	34.6	34.0	--	--
8687	34.2	34.4	33.9	35.2	35.1	--	--
8669	34.7	34.3	34.9	34.4	35.3	--	--
8673	34.3	35.2	34.1	35.3	35.1	--	--
8667	34.8	34.8	34.8	34.8	36.0	34.4	33.3
8654	34.7	35.4	35.5	35.2	35.4	34.7	35.2
8680	34.2	34.4	34.4	34.7	34.6	34.5	33.6
8676	34.8	34.7	34.4	35.1	34.8	34.8	34.8

MEAN	34.5	34.7	34.5	34.9	35.0	34.6	34.2
SD	0.29	0.44	0.52	0.33	0.59	0.18	0.92
N	8	8	8	8	8	4	4

GROUP: 2-M:0.1 mg base/kg/day

8685	34.9	34.6	34.2	34.7	35.0	--	--
8663	35.5	35.2	34.3	36.0	35.5	--	--
8686	35.0	35.4	35.6	35.6	35.6	--	--
8665	35.5	35.8	34.6	35.4	35.5	34.5	35.0
8666	35.6	34.7	34.6	35.8	35.5	35.2	34.7
8655	35.2	35.5	35.0	31.1	35.6	35.4	35.1
8659	34.5	35.5	34.6	31.0	34.8	34.6	34.5
8677	34.1	34.3	34.7	34.7	35.3	--	--

MEAN	35.0	35.1	34.7	34.3	35.4	34.9	34.8
SD	0.53	0.53	0.44	2.05	0.30	0.44	0.28
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Mean Corpus. Hemo. Conc.

STUDY ID: UIC-18

SEX: MALE

STUDY NO: 193

ABBR: MCHC

UNITS: g/dL

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
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GROUP: 3-M:0.3 mg base/kg/day

8674	34.6	35.3	35.6	35.4	35.8	34.5	35.3
8653	35.2	35.1	33.9	34.5	36.0	--	--
8660	34.4	35.0	35.1	34.8	34.7	--	--
8668	33.9	34.0	34.4	34.1	34.1	--	--
8682	34.1	33.3	33.3	31.0	33.9	33.9	34.1
8684	34.8	34.1	34.2	34.0	34.4	--	--
8662	34.7	35.0	34.5	35.0	35.4	34.2	34.8
8688	34.5	35.1	34.6	34.4	35.2	34.3	34.8

MEAN	34.5	34.6	34.5	34.2	34.9	34.2	34.8
SD	0.41	0.72	0.70	1.35	0.78	0.25	0.49
N	8	8	8	8	8	4	4

GROUP: 4-M:1.0 mg base/kg/day

8661	34.4	34.2	33.9	34.4	35.3	--	--
8670	35.2	34.6	33.7	34.3	34.6	--	--
8681	34.2	33.8	33.6	33.7	34.5	--	--
8664	35.2	34.5	34.1	32.6	34.6	--	--
8675	34.3	34.7	33.4	34.2	34.9	33.1	34.3
8683	34.3	34.5	33.5	33.7	34.1	33.8	34.8
8658	34.2	34.0	34.3	34.8	35.1	34.1	34.1
8652	35.0	34.8	33.7	34.4	34.5	34.1	34.3

MEAN	34.6	34.4	33.8	34.0	34.7	33.8	34.4
SD	0.45	0.35	0.31	0.68	0.38	0.47	0.30
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Reticulocytes

STUDY ID: UIC-18
STUDY NO: 193
ABBR: RETICS

SEX: MALE

UNITS: % RBCs

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
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GROUP: 1-M:0 mg base/kg/day

8656	0.2	0.1	0.2	0.1	0.2	--	--
8687	0.2	0.3	0.4	0.0	0.4	--	--
8669	0.1	0.2	0.8	0.2	0.3	--	--
8673	0.2	0.3	0.1	0.8	0.3	--	--
8667	0.3	0.4	0.4	1.0	0.4	0.7	0.2
8654	0.5	0.4	0.5	0.9	0.7	0.5	0.9
8680	0.4	0.4	0.3	0.5	0.4	0.3	0.2
8676	0.2	0.5	0.3	1.0	0.5	0.2	0.9

MEAN	0.3	0.3	0.4	0.6	0.4	0.4	0.6
SD	0.13	0.13	0.21	0.42	0.15	0.22	0.40
N	8	8	8	8	8	4	4

GROUP: 2-M:0.1 mg base/kg/day

8685	0.0	0.1	0.6	0.5	0.6	--	--
8663	0.0	0.4	0.4	0.2	0.5	--	--
8686	0.6	0.7	0.5	0.4	0.6	--	--
8665	0.4	0.5	0.3	1.3	0.5	0.2	0.2
8666	0.4	0.4	0.4	0.2	0.1	0.0	0.3
8655	0.0	0.3	0.4	0.7	0.1	0.1	0.0
8659	0.2	0.2	0.5	0.5	1.3	0.3	0.2
8677	0.5	0.3	1.1	0.4	0.7	--	--

MEAN	0.3	0.4	0.5	0.5	0.6	0.2	0.2
SD	0.24	0.18	0.25	0.35	0.38	0.13	0.13
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Reticulocytes

STUDY ID: UIC-18
STUDY NO: 193
ABBR: RETICS

SEX: MALE

UNITS: % RBCs

Animal ID WEEK -3 WEEK -1 WEEK 4 WEEK 8 WEEK 13 WEEK 18 WEEK 26

GROUP: 3-M:0.3 mg base/kg/day

8674	0.6	0.7	1.1	0.7	0.9	0.9	0.5
8653	0.2	0.2	0.8	0.8	0.5	--	--
8660	0.3	0.5	0.6	0.7	0.5	--	--
8668	0.1	0.1	1.3	0.6	0.5	--	--
8682	0.1	0.3	0.3	0.8	0.5	0.5	0.1
8684	0.0	0.4	0.7	0.4	0.8	--	--
8662	0.7	0.2	1.4	1.5	0.9	0.3	0.7
8688	0.3	0.0	0.6	0.6	0.5	0.2	0.2
MEAN	0.3	0.3	0.9	0.8	0.6	0.5	0.4
SD	0.25	0.23	0.38	0.32	0.19	0.31	0.28
N	8	8	8	8	8	4	4

GROUP: 4-M:1.0 mg base/kg/day

8661	0.0	0.2	0.9	0.8	0.5	--	--
8670	0.1	0.4	1.2	1.5	1.5	--	--
8681	0.3	0.9	1.4	1.4	0.9	--	--
8664	0.3	0.6	1.2	1.6	0.8	--	--
8675	0.2	0.3	2.0	1.2	0.7	0.4	0.2
8683	0.5	0.3	0.9	1.1	0.2	0.2	0.3
8658	0.2	0.7	1.2	1.6	1.3	0.4	0.4
8652	0.5	0.3	1.5	0.9	0.5	0.6	0.4
MEAN	0.3	0.5	1.3	1.3	0.8	0.4	0.3
SD	0.18	0.24	0.36	0.31	0.43	0.16	0.10
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Nucleated Red Cells

STUDY ID: UIC-18
STUDY NO: 193
ABBR: NRBC

SEX: MALE

UNITS: COUNT

Animal ID	WEEK 4	WEEK -3	WEEK -1	WEEK 8	WEEK 13	WEEK 18	WEEK 26
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GROUP: 1-M:0 mg base/kg/day

8656	0	0	0	0	0	--	--
8687	0	0	0	0	0	--	--
8669	0	0	0	0	0	--	--
8673	0	0	0	0	0	--	--
8667	0	0	0	0	0	0	0
8654	0	0	1	0	0	0	0
8680	0	1	0	0	0	0	0
8676	0	0	0	0	0	0	0

MEAN	0	0	0	0	0	0	0
SD	0.0	0.4	0.4	0.0	0.0	0.0	0.0
N	8	8	8	8	8	4	4

GROUP: 2-M:0.1 mg base/kg/day

8685	0	0	0	0	0	--	--
8663	0	0	0	0	0	--	--
8686	0	0	0	0	0	--	--
8665	0	0	0	0	0	0	0
8666	0	0	0	0	0	0	0
8655	0	0	0	0	0	0	0
8659	0	0	0	0	0	0	0
8677	0	2	0	0	0	--	--

MEAN	0	0	0	0	0	0	0
SD	0.0	0.7	0.0	0.0	0.0	0.0	0.0
N	8	8	8	8	8	4	4

WBC corrected for NRBC = or > 10

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Nucleated Red Cells

STUDY ID: UIC-18
STUDY NO: 193
ABBR: NRBC

SEX: MALE

UNITS: COUNT

Animal ID	WEEK 4	WEEK -3	WEEK -1	WEEK 8	WEEK 13	WEEK 18	WEEK 26
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GROUP: 3-M:0.3 mg base/kg/day

8674	0	0	0	0	0	0	0
8653	0	0	0	0	0	--	--
8660	0	0	0	0	0	--	--
8668	1	0	0	0	0	--	--
8682	0	0	0	0	0	0	0
8684	0	0	0	0	0	--	--
8662	0	0	0	0	1	0	0
8688	0	0	0	0	0	0	0

MEAN	0	0	0	0	0	0	0
SD	0.4	0.0	0.0	0.0	0.4	0.0	0.0
N	8	8	8	8	8	4	4

GROUP: 4-M:1.0 mg base/kg/day

8661	0	0	0	0	0	--	--
8670	1	0	0	0	0	--	--
8681	0	0	0	0	0	--	--
8664	0	0	1	0	0	--	--
8675	0	0	0	0	0	0	0
8683	2	0	0	1	0	0	0
8658	1	0	0	0	0	0	0
8652	2	0	--	0	0	0	0

MEAN	1	0	0	0	0	0	0
SD	0.9	0.0	0.4	0.4	0.0	0.0	0.0
N	8	8	7	8	8	4	4

WBC corrected for NRBC = or > 10

(--)- Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Heinz Bodies

STUDY ID: UIC-18
STUDY NO: 193
ABBR: HEINZ BOD.

SEX: MALE

UNITS: % RBCs

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
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GROUP: 1-M:0 mg base/kg/day

8656	0.0	0.0	0.0	0.0	0.0	--	--
8687	0.0	0.0	0.0	0.0	0.0	--	--
8669	0.0	0.0	0.0	0.0	0.0	--	--
8673	0.0	0.0	0.0	0.0	0.0	--	--
8667	0.0	0.0	0.0	0.0	0.0	0.0	0.0
8654	0.0	0.0	0.0	0.0	0.0	0.0	0.0
8680	0.0	0.0	0.0	0.1	0.0	0.0	0.0
8676	0.0	0.0	0.0	0.0	0.0	0.0	0.0

MEAN	0.0	0.0	0.0	0.0	0.0	0.0	0.0
SD	0.00	0.00	0.00	0.04	0.00	0.00	0.00
N	8	8	8	8	8	4	4

GROUP: 2-M:0.1 mg base/kg/day

8685	0.0	0.0	0.0	0.0	0.0	--	--
8663	0.0	0.0	0.0	0.0	0.0	--	--
8686	0.0	0.0	0.0	0.0	0.0	--	--
8665	0.0	0.0	0.0	0.0	0.0	0.1	0.0
8666	0.0	0.0	0.0	0.0	0.0	0.0	0.0
8655	0.0	0.0	0.0	0.0	0.0	0.0	0.0
8659	0.0	0.0	0.0	0.0	0.0	0.0	0.1
8677	0.0	0.0	0.0	0.0	0.0	--	--

MEAN	0.0	0.0	0.0	0.0	0.0	0.0	0.0
SD	0.00	0.00	0.00	0.00	0.00	0.05	0.05
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Heinz Bodies

STUDY ID: UIC-18

SEX: MALE

STUDY NO: 193

ABBR: HEINZ BOD.

UNITS: % RBCs

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
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GROUP: 3-M:0.3 mg base/kg/day

8674	0.0	0.0	0.0	0.0	0.0	0.0	0.0
8653	0.0	0.0	0.0	0.0	0.0	--	--
8660	0.0	0.0	0.0	0.1	0.1	--	--
8668	0.0	0.0	0.0	0.0	0.0	--	--
8682	0.0	0.0	0.0	0.0	0.0	0.0	0.0
8684	0.0	0.0	0.0	0.0	0.0	--	--
8662	0.0	0.0	0.0	0.0	0.0	0.0	0.0
8688	0.0	0.0	0.0	0.0	0.0	0.0	0.0

MEAN	0.0	0.0	0.0	0.0	0.0	0.0	0.0
SD	0.00	0.00	0.00	0.04	0.04	0.00	0.00
N	8	8	8	8	8	4	4

GROUP: 4-M:1.0 mg base/kg/day

8661	0.0	0.0	0.0	0.0	0.0	--	--
8670	0.0	0.0	0.0	0.0	0.0	--	--
8681	0.0	0.0	0.0	0.0	0.0	--	--
8664	0.0	0.0	0.0	0.0	0.0	--	--
8675	0.0	0.0	0.0	0.0	0.0	0.0	0.0
8683	0.0	0.0	0.0	0.0	0.0	0.0	0.0
8658	0.0	0.0	0.0	0.0	0.0	0.0	0.0
8652	0.0	0.0	0.0	0.0	0.0	0.0	0.0

MEAN	0.0	0.0	0.0	0.0	0.0	0.0	0.0
SD	0.00	0.00	0.00	0.00	0.00	0.00	0.00
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: % Methemoglobin

STUDY ID: UIC-18
STUDY NO: 193
ABBR: % METHGB

SEX: MALE

UNITS: % HGBs

Animal ID WEEK -3 WEEK -1 WEEK 4 WEEK 8 WEEK 13 WEEK 18 WEEK 26

GROUP: 1-M:0 mg base/kg/day

8656	0.4	0.9	0.6	0.7	0.3	--	--
8687	0.3	0.5	0.5	0.7	0.8	--	--
8669	2.5	1.4	1.6	0.3	0.5	--	--
8673	0.5	0.4	0.9	0.8	0.7	--	--
8667	3.0	2.0	1.9	1.0	0.6	0.7	0.8
8654	1.1	1.5	1.2	1.1	0.4	0.4	0.6
8680	0.6	0.3	0.7	0.8	0.4	0.4	0.8
8676	2.5	3.2	3.6	1.7	0.6	0.7	0.6

MEAN	1.4	1.3	1.4	0.9	0.5	0.6	0.7
SD	1.12	0.98	1.03	0.41	0.17	0.17	0.12
N	8	8	8	8	8	4	4

GROUP: 2-M:0.1 mg base/kg/day

8685	0.4	0.6	2.5	1.6	1.5	--	--
8663	3.0	2.3	1.7	1.3	1.2	--	--
8686	0.9	0.6	2.7	2.0	1.4	--	--
8665	0.9	1.0	3.6	2.0	2.2	0.6	0.6
8666	1.7	1.7	2.8	1.8	1.9	0.3	0.7
8655	1.4	0.5	2.0	1.9	1.4	0.6	0.7
8659	1.9	1.4	3.2	2.1	1.5	0.5	0.6
8677	2.3	3.5	4.7	1.8	2.7	--	--

MEAN	1.6	1.5	2.9	1.8	1.7	0.5	0.7
SD	0.85	1.04	0.95	0.26	0.51	0.14	0.06
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: % Methemoglobin

STUDY ID: UIC-18
STUDY NO: 193
ABBR: % METHGB

SEX: MALE

UNITS: % HGBs

Animal ID WEEK -3 WEEK -1 WEEK 4 WEEK 8 WEEK 13 WEEK 18 WEEK 26

GROUP: 3-M:0.3 mg base/kg/day

8674	0.4	0.8	9.9	6.4	5.2	0.5	0.6
8653	2.3	1.7	9.2	5.7	5.9	--	--
8660	0.5	0.3	10.1	7.2	5.9	--	--
8668	0.8	0.6	10.7	7.2	7.8	--	--
8682	1.9	1.9	7.4	4.1	8.1	0.6	0.6
8684	1.4	1.6	9.3	6.3	6.1	--	--
8662	1.5	0.9	11.9	7.9	7.4	0.5	0.9
8688	1.7	1.8	7.4	4.8	4.1	0.8	0.9

MEAN	1.3	1.2	9.5	6.2	6.3	0.6	0.8
SD	0.68	0.62	1.54	1.29	1.37	0.14	0.17
N	8	8	8	8	8	4	4

GROUP: 4-M:1.0 mg base/kg/day

8661	1.0	0.8	24.1	19.4	14.5	--	--
8670	0.2	0.9	23.8	18.9	16.0	--	--
8681	1.2	1.7	28.6	21.7	19.9	--	--
8664	0.6	0.6	28.4	20.7	18.9	--	--
8675	1.3	0.4	35.6	34.2	30.9	0.7	0.6
8683	0.3	0.4	23.1	19.4	18.9	0.9	0.7
8658	0.5	0.8	28.7	17.9	22.7	0.8	0.8
8652	2.2	2.8	27.5	19.7	18.6	1.9	0.7

MEAN	0.9	1.1	27.5	21.5	20.1	1.1	0.7
SD	0.66	0.82	4.03	5.26	5.02	0.56	0.08
N	8	8	8	8	8	4	4

(--) - Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Platelets

STUDY ID: UIC-18

SEX: MALE

STUDY NO: 193

ABBR: PLT

UNITS: $10^3/\text{mm}^3$

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
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GROUP: 1-M:0 mg base/kg/day

8656	247	201	233	168	191	--	--
8687	231	189	189	188	179	--	--
8669	247	193	178	208	201	--	--
8673	319	228	220	192	212	--	--
8667	297	197	212	214	105	223	176
8654	300	260	258	291	266	264	251
8680	253	194	197	211	211	202	201
8676	319	243	248	261	231	220	233

MEAN	277	213	217	217	200	227	215
SD	35.8	26.9	28.4	40.4	46.5	26.2	33.4
N	8	8	8	8	8	4	4

GROUP: 2-M:0.1 mg base/kg/day

8685	278	226	172	180	188	--	--
8663	455	343	292	270	238	--	--
8686	320	275	171	238	222	--	--
8665	336	244	229	220	151	215	209
8666	302	207	180	149	189	252	243
8655	369	300	266	132	257	269	273
8659	322	265	174	95	137	213	197
8677	436	318	269	221	244	--	--

MEAN	352	272	219	188	203	237	231
SD	63.4	46.5	51.0	59.4	44.2	27.7	34.4
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Platelets

STUDY ID: UIC-18
STUDY NO: 193
ABBR: PLT

SEX: MALE

UNITS: $10^3/\text{mm}^3$

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
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GROUP: 3-M:0.3 mg base/kg/day

8674	247	236	90	141	119	224	233
8653	290	220	99	111	195	--	--
8660	321	248	110	146	132	--	--
8668	159	145	77	130	98	--	--
8682	178	168	79	79	64	215	189
8684	153	157	110	156	147	--	--
8662	425	232	81	160	168	255	271
8688	263	207	110	153	146	224	192

MEAN	255	202	95	135	134	230	221
SD	92.7	39.6	14.6	27.5	40.7	17.5	38.8
N	8	8	8	8	8	4	4

GROUP: 4-M:1.0 mg base/kg/day

8661	293	246	52	135	185	--	--
8670	378	271	97	159	195	--	--
8681	323	258	50	150	151	--	--
8664	308	259	56	113	143	--	--
8675	300	203	84	174	185	221	195
8683	330	279	95	169	192	315	161
8658	330	229	89	151	126	351	257
8652	323	249	60	95	103	258	226

MEAN	323	249	73	143	160	286	210
SD	26.1	24.2	20.2	27.4	34.4	58.0	41.2
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Prothrombin Time

STUDY ID: UIC-18
STUDY NO: 193
ABBR: PT

SEX: MALE

UNITS: sec

Animal ID WEEK -3 WEEK -1 WEEK 4 WEEK 8 WEEK 13 WEEK 18 WEEK 26

GROUP: 1-M:0 mg base/kg/day

8656	8.0	8.3	8.4	8.4	10.9	--	--
8687	8.4	8.3	8.5	8.5	9.6	--	--
8669	7.7	8.0	8.1	8.1	8.9	--	--
8673	9.4	9.4	9.5	9.3	9.2	--	--
8667	9.1	9.0	9.2	9.5	9.2	9.3	8.9
8654	8.0	8.0	8.2	7.9	8.0	8.0	7.7
8680	8.1	7.9	8.1	7.9	8.2	8.4	8.2
8676	8.2	8.2	8.2	8.4	10.3	8.3	8.2

MEAN	8.4	8.4	8.5	8.5	9.3	8.5	8.3
SD	0.59	0.53	0.53	0.60	0.98	0.56	0.49
N	8	8	8	8	8	4	4

GROUP: 2-M:0.1 mg base/kg/day

8685	8.5	8.5	8.0	8.6	8.5	--	--
8663	8.7	8.6	8.8	8.8	8.6	--	--
8686	8.2	8.2	8.1	8.3	8.0	--	--
8665	8.4	7.9	8.1	8.4	8.3	8.4	8.2
8666	8.5	8.0	8.5	8.2	8.2	8.2	8.0
8655	8.0	8.1	8.3	8.5	8.2	8.3	7.9
8659	8.1	8.1	8.1	8.4	8.3	8.4	8.0
8677	8.2	8.5	8.6	8.6	8.6	--	--

MEAN	8.3	8.2	8.3	8.5	8.3	8.3	8.0
SD	0.24	0.26	0.29	0.19	0.21	0.10	0.13
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Prothrombin Time

STUDY ID: UIC-18
STUDY NO: 193
ABBR: PT

SEX: MALE

UNITS: sec

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
GROUP: 3-M:0.3 mg base/kg/day							
8674	8.2	8.1	8.3	7.9	9.4	8.2	8.0
8653	8.1	8.0	8.2	8.2	8.0	--	--
8660	8.1	7.8	7.8	7.8	8.2	--	--
8668	7.9	8.1	8.0	8.1	8.1	--	--
8682	8.5	8.1	8.3	8.2	10.6	8.1	7.8
8684	8.8	8.6	8.6	8.9	8.9	--	--
8662	8.4	8.2	8.2	8.0	8.1	8.3	7.8
8688	8.3	7.9	9.8	8.2	8.2	8.3	8.0
MEAN	8.3	8.1	8.4	8.2	8.7	8.2	7.9
SD	0.28	0.24	0.61	0.33	0.91	0.10	0.12
N	8	8	8	8	8	4	4

GROUP: 4-M:1.0 mg base/kg/day							
8661	8.5	8.3	8.1	8.3	8.1	--	--
8670	8.1	8.0	8.0	8.1	7.9	--	--
8681	8.4	8.3	7.8	8.3	8.0	--	--
8664	8.3	8.0	7.8	8.3	8.1	--	--
8675	8.3	8.1	8.0	8.2	7.9	8.2	7.8
8683	8.5	8.4	7.9	8.3	8.1	8.5	7.8
8658	8.1	8.1	8.0	7.9	7.8	8.3	7.9
8652	8.9	9.2	10.0	9.2	8.9	9.4	8.9
MEAN	8.4	8.3	8.2	8.3	8.1	8.6	8.1
SD	0.26	0.39	0.73	0.38	0.34	0.55	0.54
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Act. Partial Thrombo. Time

STUDY ID: UIC-18
STUDY NO: 193
ABBR: APTT

SEX: MALE

UNITS: sec

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
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GROUP: 1-M:0 mg base/kg/day

8656	12.3	11.6	10.8	11.5	8.2	--	--
8687	10.3	9.6	9.4	9.9	8.4	--	--
8669	10.4	9.6	9.6	9.3	8.9	--	--
8673	9.8	9.9	9.2	9.4	8.9	--	--
8667	10.0	9.8	9.0	9.8	9.9	9.5	9.3
8654	10.3	10.1	9.8	9.9	9.5	9.5	9.1
8680	12.0	10.8	10.2	11.1	10.4	10.4	10.6
8676	11.2	10.6	10.6	10.5	8.3	9.6	9.9
MEAN	10.8	10.3	9.8	10.2	9.1	9.8	9.7
SD	0.94	0.70	0.65	0.79	0.80	0.44	0.68
N	8	8	8	8	8	4	4

GROUP: 2-M:0.1 mg base/kg/day

8685	9.6	9.1	9.3	9.5	9.4	--	--
8663	12.6	11.8	11.5	11.8	11.9	--	--
8686	10.0	9.5	9.4	9.7	9.9	--	--
8665	9.8	9.7	9.5	9.6	9.3	9.5	10.0
8666	10.3	10.3	9.6	9.9	9.3	9.3	9.3
8655	10.1	9.9	9.6	10.2	9.6	9.8	9.6
8659	10.3	9.8	9.3	10.0	9.4	9.1	9.5
8677	10.8	10.0	9.7	10.5	10.1	--	--
MEAN	10.4	10.0	9.7	10.2	9.9	9.4	9.6
SD	0.95	0.80	0.73	0.74	0.87	0.30	0.29
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Act. Partial Thrombo. Time

STUDY ID: UIC-18
STUDY NO: 193
ABBR: APTT

SEX: MALE

UNITS: sec

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
GROUP: 3-M:0.3 mg base/kg/day							
8674	10.3	10.5	9.5	9.9	8.2	8.3	9.2
8653	10.1	9.8	9.7	10.2	9.6	--	--
8660	10.5	10.4	10.4	9.7	9.6	--	--
8668	10.5	10.1	10.3	10.4	9.8	--	--
8682	10.9	10.3	10.4	11.2	8.2	10.0	10.2
8684	10.2	11.4	9.5	9.7	10.9	--	--
8662	10.2	9.9	9.2	9.9	10.2	9.5	9.6
8688	10.6	10.2	8.1	10.2	9.8	10.0	9.7
MEAN	10.4	10.3	9.6	10.2	9.5	9.5	9.7
SD	0.26	0.49	0.77	0.49	0.93	0.80	0.41
N	8	8	8	8	8	4	4

GROUP: 4-M:1.0 mg base/kg/day							
8661	12.6	11.7	11.3	12.1	11.5	--	--
8670	10.2	9.8	10.1	9.8	9.9	--	--
8681	11.1	10.7	10.6	10.3	9.9	--	--
8664	12.4	11.7	11.6	12.9	11.1	--	--
8675	13.4	12.2	11.7	12.7	11.9	11.4	11.8
8683	10.2	10.1	9.8	10.4	9.8	9.6	10.1
8658	11.1	14.0	10.5	10.8	10.4	10.4	10.7
8652	11.2	9.6	8.5	10.1	10.1	9.9	11.8
MEAN	11.5	11.2	10.5	11.1	10.6	10.3	11.1
SD	1.16	1.48	1.07	1.24	0.82	0.79	0.84
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Leukocytes

STUDY ID: UIC-18
STUDY NO: 193
ABBR: WBC

SEX: MALE

UNITS: $10^3/\text{mm}^3$

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
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GROUP: 1-M:0 mg base/kg/day

8656	6.8	8.7	9.3	10.3	14.2	--	--
8687	6.9	10.9	7.6	7.6	7.2	--	--
8669	7.9	9.4	11.6	6.9	7.6	--	--
8673	6.1	6.7	7.2	5.7	6.9	--	--
8667	8.3	11.0	9.5	9.0	9.6	8.4	7.8
8654	5.9	7.8	7.2	8.1	8.1	6.1	6.8
8680	8.7	13.2	10.0	12.3	9.6	9.4	9.1
8676	5.9	6.6	9.0	7.4	7.8	7.5	7.2

MEAN	7.1	9.3	8.9	8.4	8.9	7.9	7.7
SD	1.11	2.31	1.54	2.09	2.38	1.40	1.00
N	8	8	8	8	8	4	4

GROUP: 2-M:0.1 mg base/kg/day

8685	6.4	7.5	7.3	6.5	6.9	--	--
8663	6.0	7.5	6.9	6.5	7.3	--	--
8686	6.1	11.3	8.6	7.3	8.4	--	--
8665	6.4	9.1	7.8	7.2	7.7	9.1	8.7
8666	7.4	8.9	8.8	8.5	8.8	7.5	7.5
8655	6.7	6.8	8.1	5.9	6.7	6.3	8.4
8659	7.2	10.0	8.9	9.1	9.6	8.3	8.2
8677	7.9	12.0	9.3	9.1	9.0	--	--

MEAN	6.8	9.1	8.2	7.5	8.1	7.8	8.2
SD	0.67	1.87	0.84	1.24	1.06	1.19	0.51
N	8	8	8	8	8	4	4

WBC corrected for NRBC = or > 10

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Leukocytes

STUDY ID: UIC-18
STUDY NO: 193
ABBR: WBC

SEX: MALE

UNITS: $10^3/\text{mm}^3$

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
GROUP: 3-M:0.3 mg base/kg/day							
8674	7.9	9.5	8.8	11.2	7.7	7.0	7.5
8653	7.6	13.9	9.6	5.6	8.4	--	--
8660	7.1	11.1	11.1	7.7	9.8	--	--
8668	5.6	9.6	12.7	11.6	10.8	--	--
8682	4.5	6.0	5.7	6.3	6.5	4.9	4.1
8684	7.6	10.6	14.7	10.7	10.6	--	--
8662	8.7	7.7	11.6	9.2	9.0	6.9	7.5
8688	7.2	7.2	6.7	7.7	6.7	6.9	5.8
MEAN	7.0	9.5	10.1	8.8	8.7	6.4	6.2
SD	1.35	2.50	3.02	2.28	1.66	1.02	1.63
N	8	8	8	8	8	4	4

GROUP: 4-M:1.0 mg base/kg/day							
8661	6.1	6.6	10.4	7.8	9.4	--	--
8670	7.2	12.7	10.0	12.1	14.3	--	--
8681	7.8	8.7	8.7	12.6	11.1	--	--
8664	6.8	10.5	10.0	9.0	9.6	--	--
8675	6.3	6.8	7.8	8.2	7.7	5.5	6.8
8683	9.9	8.9	12.4	11.1	14.5	5.7	8.1
8658	6.8	9.6	10.7	10.0	9.3	9.0	7.3
8652	9.8	13.6	16.3	27.0	23.7	11.3	13.7
MEAN	7.6	9.7	10.8	12.2	12.5	7.9	9.0
SD	1.49	2.52	2.61	6.22	5.15	2.79	3.20
N	8	8	8	8	8	4	4

WBC corrected for NRBC = or > 10

(--) - Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18		GROUP: 1-M : 0 mg base/kg/day						SEX: MALE	
STUDY NO: 193									
Animal ID		WEEK -3		WEEK -1		WEEK 4		WEEK 8	
		REL	ABS	REL	ABS	REL	ABS	REL	ABS
8656	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	71.0	4.8	70.0	6.1	86.0	8.0	75.0	7.7
	I. Neutrophils	0.0	0.0	0.0	0.0	1.0	0.1	0.0	0.0
	Lymphocytes	17.0	1.2	19.0	1.7	8.0	0.7	18.0	1.9
	Monocytes	8.0	0.5	4.0	0.3	5.0	0.5	3.0	0.3
	Eosinophils	4.0	0.3	7.0	0.6	0.0	0.0	4.0	0.4
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		6.8		8.7		9.3		10.3
8687	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	38.0	2.6	62.0	6.8	68.0	5.2	60.0	4.6
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	51.0	3.5	32.0	3.5	27.0	2.1	37.0	2.8
	Monocytes	6.0	0.4	4.0	0.4	3.0	0.2	1.0	0.1
	Eosinophils	5.0	0.3	2.0	0.2	2.0	0.2	2.0	0.2
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		6.9		10.9		7.6		7.6
8669	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	58.0	4.6	64.0	6.0	66.0	7.7	58.0	4.0
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	26.0	2.1	34.0	3.2	26.0	3.0	37.0	2.6
	Monocytes	10.0	0.8	2.0	0.2	7.0	0.8	3.0	0.2
	Eosinophils	6.0	0.5	0.0	0.0	1.0	0.1	2.0	0.1
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		7.9		9.4		11.6		6.9

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18

STUDY NO: 193

GROUP: 1-M : 0 mg base/kg/day

SEX: MALE

Animal ID		WEEK -3		WEEK -1		WEEK 4		WEEK 8	
		REL	ABS	REL	ABS	REL	ABS	REL	ABS
8673	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	57.0	3.5	63.0	4.2	57.0	4.1	71.0	4.0
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	38.0	2.3	26.0	1.7	34.0	2.4	26.0	1.5
	Monocytes	4.0	0.2	9.0	0.6	7.0	0.5	3.0	0.2
	Eosinophils	1.0	0.1	2.0	0.1	2.0	0.1	0.0	0.0
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		6.1		6.7		7.2		5.7
8667	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	52.0	4.3	57.0	6.3	65.0	6.2	71.0	6.4
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	39.0	3.2	39.0	4.3	25.0	2.4	24.0	2.2
	Monocytes	6.0	0.5	3.0	0.3	3.0	0.3	1.0	0.1
	Eosinophils	3.0	0.2	1.0	0.1	7.0	0.7	4.0	0.4
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		8.3		11.0		9.5		9.0
8654	Nucleated Red Cells	0		1		0		0	
	M. Neutrophils	68.0	4.0	71.0	5.5	75.0	5.4	84.0	6.8
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	22.0	1.3	17.0	1.3	14.0	1.0	14.0	1.1
	Monocytes	8.0	0.5	9.0	0.7	10.0	0.7	2.0	0.2
	Eosinophils	2.0	0.1	3.0	0.2	1.0	0.1	0.0	0.0
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		5.9		7.8		7.2		8.1

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18

STUDY NO: 193

GROUP: 1-M : 0 mg base/kg/day

SEX: MALE

Animal ID		WEEK -3		WEEK -1		WEEK 4		WEEK 8	
		REL	ABS	REL	ABS	REL	ABS	REL	ABS
8680	Nucleated Red Cells	1		0		0		0	
	M. Neutrophils	59.0	5.1	70.0	9.2	64.0	6.4	73.0	9.0
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	29.0	2.5	21.0	2.8	29.0	2.9	21.0	2.6
	Monocytes	6.0	0.5	8.0	1.1	7.0	0.7	4.0	0.5
	Eosinophils	6.0	0.5	1.0	0.1	0.0	0.0	2.0	0.2
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		8.7		13.2		10.0		12.3
8676	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	52.0	3.1	53.0	3.5	70.0	6.3	66.0	4.9
	I. Neutrophils	0.0	0.0	2.0	0.1	0.0	0.0	0.0	0.0
	Lymphocytes	35.0	2.1	38.0	2.5	23.0	2.1	22.0	1.6
	Monocytes	3.0	0.2	4.0	0.3	5.0	0.5	4.0	0.3
	Eosinophils	10.0	0.6	3.0	0.2	2.0	0.2	8.0	0.6
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		5.9		6.6		9.0		7.4

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18

STUDY NO: 193

GROUP: 2-M : 0.1 mg base/kg/day

SEX: MALE

Animal ID		WEEK -3		WEEK -1		WEEK 4		WEEK 8	
		REL	ABS	REL	ABS	REL	ABS	REL	ABS
8685	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	63.0	4.0	60.0	4.5	60.0	4.4	65.0	4.2
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	31.0	2.0	38.0	2.9	29.0	2.1	30.0	2.0
	Monocytes	5.0	0.3	2.0	0.2	7.0	0.5	2.0	0.1
	Eosinophils	1.0	0.1	0.0	0.0	4.0	0.3	3.0	0.2
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		6.4		7.5		7.3		6.5
8683	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	44.0	2.6	67.0	5.0	59.0	4.1	51.0	3.3
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	43.0	2.6	25.0	1.9	27.0	1.9	36.0	2.3
	Monocytes	3.0	0.2	4.0	0.3	6.0	0.4	5.0	0.3
	Eosinophils	10.0	0.6	4.0	0.3	8.0	0.6	8.0	0.5
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		6.0		7.5		6.9		6.5
8686	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	60.0	3.7	84.0	9.5	71.0	6.1	73.0	5.3
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	33.0	2.0	13.0	1.5	17.0	1.5	27.0	2.0
	Monocytes	7.0	0.4	3.0	0.3	11.0	0.9	0.0	0.0
	Eosinophils	0.0	0.0	0.0	0.0	1.0	0.1	0.0	0.0
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		6.1		11.3		8.6		7.3

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18

STUDY NO: 193

GROUP: 2-M : 0.1 mg base/kg/day

SEX: MALE

Animal ID		WEEK -3		WEEK -1		WEEK 4		WEEK 8	
		REL	ABS	REL	ABS	REL	ABS	REL	ABS
8665	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	56.0	3.6	76.0	6.9	64.0	5.0	69.0	5.0
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	27.0	1.7	13.0	1.2	23.0	1.8	28.0	2.0
	Monocytes	10.0	0.6	9.0	0.8	8.0	0.6	1.0	0.1
	Eosinophils	7.0	0.4	2.0	0.2	5.0	0.4	2.0	0.1
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		6.4		9.1		7.8		7.2
8666	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	50.0	3.7	66.0	5.9	56.0	4.9	69.0	5.9
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	33.0	2.4	22.0	2.0	35.0	3.1	22.0	1.9
	Monocytes	5.0	0.4	6.0	0.5	4.0	0.4	5.0	0.4
	Eosinophils	12.0	0.9	6.0	0.5	5.0	0.4	4.0	0.3
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		7.4		8.9		8.8		8.5
8655	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	53.0	3.6	53.0	3.6	70.0	5.7	56.0	3.3
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	38.0	2.5	44.0	3.0	27.0	2.2	33.0	1.9
	Monocytes	7.0	0.5	0.0	0.0	3.0	0.2	7.0	0.4
	Eosinophils	2.0	0.1	3.0	0.2	0.0	0.0	4.0	0.2
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		6.7		6.8		8.1		5.9

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18		GROUP: 2-M : 0.1 mg base/kg/day						SEX: MALE	
STUDY NO: 193									
Animal ID		WEEK -3		WEEK -1		WEEK 4		WEEK 8	
		REL	ABS	REL	ABS	REL	ABS	REL	ABS
8659	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	54.0	3.9	72.0	7.2	62.0	5.5	64.0	5.8
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	37.0	2.7	17.0	1.7	22.0	2.0	26.0	2.4
	Monocytes	6.0	0.4	9.0	0.9	10.0	0.9	5.0	0.5
	Eosinophils	3.0	0.2	2.0	0.2	6.0	0.5	5.0	0.5
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
WBC		7.2		10.0		8.9		9.1	
8677	Nucleated Red Cells	2		0		0		0	
	M. Neutrophils	52.0	4.1	75.0	9.0	59.0	5.5	58.0	5.3
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	31.0	2.4	20.0	2.4	36.0	3.3	33.0	3.0
	Monocytes	9.0	0.7	3.0	0.4	2.0	0.2	6.0	0.5
	Eosinophils	8.0	0.6	2.0	0.2	3.0	0.3	3.0	0.3
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
WBC		7.9		12.0		9.3		9.1	

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18

STUDY NO: 193

GROUP: 3-M : 0.3 mg base/kg/day

SEX: MALE

Animal ID		WEEK -3		WEEK -1		WEEK 4		WEEK 8	
		REL	ABS	REL	ABS	REL	ABS	REL	ABS
8674	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	41.0	3.2	64.0	6.1	60.0	5.3	79.0	8.8
	I. Neutrophils	0.0	0.0	0.0	0.0	2.0	0.2	0.0	0.0
	Lymphocytes	49.0	3.9	30.0	2.9	25.0	2.2	19.0	2.1
	Monocytes	0.0	0.0	3.0	0.3	4.0	0.4	0.0	0.0
	Eosinophils	4.0	0.3	3.0	0.3	9.0	0.8	2.0	0.2
	Basophils	6.0	0.5	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		7.9		9.5		8.8		11.2
8653	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	48.0	3.6	65.0	9.0	62.0	6.0	68.0	3.8
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	38.0	2.9	27.0	3.8	29.0	2.8	26.0	1.5
	Monocytes	4.0	0.3	6.0	0.8	4.0	0.4	1.0	0.1
	Eosinophils	10.0	0.8	2.0	0.3	5.0	0.5	5.0	0.3
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		7.6		13.9		9.6		5.6
8660	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	58.0	4.1	78.0	8.7	76.0	8.4	79.0	6.1
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	29.0	2.1	15.0	1.7	16.0	1.8	18.0	1.4
	Monocytes	11.0	0.8	4.0	0.4	7.0	0.8	2.0	0.2
	Eosinophils	2.0	0.1	3.0	0.3	1.0	0.1	1.0	0.1
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		7.1		11.1		11.1		7.7

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18

STUDY NO: 193

GROUP: 3-M : 0.3 mg base/kg/day

SEX: MALE

Animal ID		WEEK -3		WEEK -1		WEEK 4		WEEK 8	
		REL	ABS	REL	ABS	REL	ABS	REL	ABS
8668	Nucleated Red Cells	0		0		1		0	
	M. Neutrophils	47.0	2.6	76.0	7.3	64.0	8.1	70.0	8.1
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	33.0	1.8	16.0	1.5	22.0	2.8	23.0	2.7
	Monocytes	10.0	0.6	6.0	0.6	9.0	1.1	3.0	0.3
	Eosinophils	10.0	0.6	2.0	0.2	5.0	0.6	4.0	0.5
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		5.6		9.6		12.7		11.6
8682	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	58.0	2.6	69.0	4.1	58.0	3.3	72.0	4.5
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	1.0	0.1
	Lymphocytes	24.0	1.1	17.0	1.0	33.0	1.9	18.0	1.1
	Monocytes	9.0	0.4	7.0	0.4	6.0	0.3	4.0	0.3
	Eosinophils	9.0	0.4	7.0	0.4	3.0	0.2	5.0	0.3
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		4.5		6.0		5.7		6.3
8684	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	54.0	4.1	70.0	7.4	70.0	10.3	56.0	6.0
	I. Neutrophils	1.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	30.0	2.3	20.0	2.1	21.0	3.1	25.0	2.7
	Monocytes	8.0	0.6	4.0	0.4	6.0	0.9	3.0	0.3
	Eosinophils	7.0	0.5	6.0	0.6	3.0	0.4	16.0	1.7
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		7.6		10.6		14.7		10.7

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18

STUDY NO: 193

GROUP: 3-M : 0.3 mg base/kg/day

SEX: MALE

Animal ID		WEEK -3		WEEK -1		WEEK 4		WEEK 8	
		REL	ABS	REL	ABS	REL	ABS	REL	ABS
8662	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	49.0	4.3	60.0	4.6	70.0	8.1	72.0	6.6
	I. Neutrophils	0.0	0.0	0.0	0.0	2.0	0.2	0.0	0.0
	Lymphocytes	39.0	3.4	34.0	2.6	25.0	2.9	23.0	2.1
	Monocytes	4.0	0.3	3.0	0.2	1.0	0.1	3.0	0.3
	Eosinophils	8.0	0.7	3.0	0.2	0.0	0.0	2.0	0.2
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	2.0	0.2	0.0	0.0
	WBC		8.7		7.7		11.6		9.2
8688	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	52.0	3.7	69.0	5.0	60.0	4.0	61.0	4.7
	I. Neutrophils	0.0	0.0	0.0	0.0	1.0	0.1	0.0	0.0
	Lymphocytes	38.0	2.7	25.0	1.8	34.0	2.3	34.0	2.6
	Monocytes	7.0	0.5	6.0	0.4	4.0	0.3	1.0	0.1
	Eosinophils	3.0	0.2	0.0	0.0	1.0	0.1	4.0	0.3
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		7.2		7.2		6.7		7.7

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18

STUDY NO: 193

GROUP: 4-M : 1.0 mg base/kg/day

SEX: MALE

Animal ID		WEEK -3		WEEK -1		WEEK 4		WEEK 8	
		REL	ABS	REL	ABS	REL	ABS	REL	ABS
8661	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	39.0	2.4	61.0	4.0	49.0	5.1	60.0	4.7
	I. Neutrophils	0.0	0.0	0.0	0.0	1.0	0.1	2.0	0.2
	Lymphocytes	48.0	2.9	28.0	1.8	40.0	4.2	28.0	2.2
	Monocytes	7.0	0.4	7.0	0.5	7.0	0.7	2.0	0.2
	Eosinophils	6.0	0.4	4.0	0.3	3.0	0.3	8.0	0.6
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		6.1		6.6		10.4		7.8
8670	Nucleated Red Cells	0		0		1		0	
	M. Neutrophils	67.0	4.8	80.0	10.2	72.0	7.2	81.0	9.8
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	23.0	1.7	13.0	1.7	17.0	1.7	14.0	1.7
	Monocytes	4.0	0.3	3.0	0.4	8.0	0.8	4.0	0.5
	Eosinophils	6.0	0.4	4.0	0.5	3.0	0.3	1.0	0.1
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		7.2		12.7		10.0		12.1
8681	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	45.0	3.5	64.0	5.6	53.0	4.6	64.0	8.1
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	44.0	3.4	30.0	2.6	36.0	3.1	28.0	3.5
	Monocytes	7.0	0.5	3.0	0.3	9.0	0.8	4.0	0.5
	Eosinophils	4.0	0.3	3.0	0.3	2.0	0.2	4.0	0.5
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		7.8		8.7		8.7		12.6

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18

STUDY NO: 193

GROUP: 4-M : 1.0 mg base/kg/day

SEX: MALE

Animal ID		WEEK -3		WEEK -1		WEEK 4		WEEK 8	
		REL	ABS	REL	ABS	REL	ABS	REL	ABS
8664	Nucleated Red Cells	0		1		0		0	
	M. Neutrophils	60.0	4.1	69.0	7.2	61.0	6.1	75.0	6.8
	I. Neutrophils	0.0	0.0	1.0	0.1	0.0	0.0	0.0	0.0
	Lymphocytes	31.0	2.1	22.0	2.3	31.0	3.1	23.0	2.1
	Monocytes	6.0	0.4	7.0	0.7	6.0	0.6	2.0	0.2
	Eosinophils	3.0	0.2	1.0	0.1	2.0	0.2	0.0	0.0
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		6.8		10.5		10.0		9.0
8675	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	50.0	3.2	61.0	4.1	70.0	5.5	65.0	5.3
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	41.0	2.6	34.0	2.3	23.0	1.8	27.0	2.2
	Monocytes	4.0	0.3	4.0	0.3	6.0	0.5	3.0	0.2
	Eosinophils	5.0	0.3	1.0	0.1	1.0	0.1	5.0	0.4
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		6.3		6.8		7.8		8.2
8683	Nucleated Red Cells	0		0		2		1	
	M. Neutrophils	49.0	4.9	51.0	4.5	53.0	6.6	62.0	6.9
	I. Neutrophils	0.0	0.0	2.0	0.2	0.0	0.0	0.0	0.0
	Lymphocytes	48.0	4.8	39.0	3.5	36.0	4.5	27.0	3.0
	Monocytes	3.0	0.3	5.0	0.4	10.0	1.2	6.0	0.7
	Eosinophils	0.0	0.0	3.0	0.3	1.0	0.1	5.0	0.6
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		9.9		8.9		12.4		11.1

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18

STUDY NO: 193

GROUP: 1-M : 0 mg base/kg/day

SEX: MALE

Animal ID		WEEK 13		WEEK 18		WEEK 26	
		REL	ABS	REL	ABS	REL	ABS
8656	Nucleated Red Cells	0		0		0	
	M. Neutrophils	82.0	11.6	0	--	0	--
	I. Neutrophils	0.0	0.0	0	--	0	--
	Lymphocytes	14.0	2.0	0	--	0	--
	Monocytes	2.0	0.3	0	--	0	--
	Eosinophils	2.0	0.3	0	--	0	--
	Basophils	0.0	0.0	0	--	0	--
	Atypical Lymphocytes	0.0	0.0	0	--	0	--
	Metamyelocytes	0.0	0.0	0	--	0	--
	WBC		14.2		--		--
8687	Nucleated Red Cells	0		0		0	
	M. Neutrophils	54.0	3.9	0	--	0	--
	I. Neutrophils	0.0	0.0	0	--	0	--
	Lymphocytes	40.0	2.9	0	--	0	--
	Monocytes	1.0	0.1	0	--	0	--
	Eosinophils	5.0	0.4	0	--	0	--
	Basophils	0.0	0.0	0	--	0	--
	Atypical Lymphocytes	0.0	0.0	0	--	0	--
	Metamyelocytes	0.0	0.0	0	--	0	--
	WBC		7.2		--		--
8669	Nucleated Red Cells	0		0		0	
	M. Neutrophils	70.0	5.3	0	--	0	--
	I. Neutrophils	0.0	0.0	0	--	0	--
	Lymphocytes	26.0	2.0	0	--	0	--
	Monocytes	2.0	0.2	0	--	0	--
	Eosinophils	2.0	0.2	0	--	0	--
	Basophils	0.0	0.0	0	--	0	--
	Atypical Lymphocytes	0.0	0.0	0	--	0	--
	Metamyelocytes	0.0	0.0	0	--	0	--
	WBC		7.6		--		--

WBC corrected for NRBC = or > 10

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY IO: UIC-18
STUDY NO: 193

GROUP: 1-M : 0 mg base/kg/day

SEX: MALE

Animal ID		WEEK 13		WEEK 18		WEEK 26	
		REL	ABS	REL	ABS	REL	ABS
8680	Nucleated Red Cells	0		0		0	
	M. Neutrophils	64.0	6.1	68.0	6.4	65.0	5.9
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	32.0	3.1	26.0	2.4	28.0	2.5
	Monocytes	3.0	0.3	4.0	0.4	3.0	0.3
	Eosinophils	1.0	0.1	2.0	0.2	4.0	0.4
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		9.6		9.4		9.1
8676	Nucleated Red Cells	0		0		0	
	M. Neutrophils	68.0	5.3	68.0	5.1	69.0	5.0
	I. Neutrophils	0.0	0.0	0.0	0.0	27.0	1.9
	Lymphocytes	24.0	1.9	27.0	2.0	1.0	0.1
	Monocytes	3.0	0.2	2.0	0.2	3.0	0.2
	Eosinophils	5.0	0.4	3.0	0.2	0.0	0.0
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		7.8		7.5		7.2

WBC corrected for NRBC = or > 10

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18

STUDY NO: 193

GROUP: 2-M : 0.1 mg base/kg/day

SEX: MALE

Animal ID		WEEK 13		WEEK 18		WEEK 26	
		REL	ABS	REL	ABS	REL	ABS
8685	Nucleated Red Cells	0		0		0	
	M. Neutrophils	64.0	4.4	0	--	0	--
	I. Neutrophils	0.0	0.0	0	--	0	--
	Lymphocytes	28.0	1.9	0	--	0	--
	Monocytes	4.0	0.3	0	--	0	--
	Eosinophils	4.0	0.3	0	--	0	--
	Basophils	0.0	0.0	0	--	0	--
	Atypical Lymphocytes	0.0	0.0	0	--	0	--
	Metamyelocytes	0.0	0.0	0	--	0	--
	WBC		6.9		--		--
8663	Nucleated Red Cells	0		0		0	
	M. Neutrophils	66.0	4.8	0	--	0	--
	I. Neutrophils	0.0	0.0	0	--	0	--
	Lymphocytes	27.0	2.0	0	--	0	--
	Monocytes	5.0	0.4	0	--	0	--
	Eosinophils	2.0	0.1	0	--	0	--
	Basophils	0.0	0.0	0	--	0	--
	Atypical Lymphocytes	0.0	0.0	0	--	0	--
	Metamyelocytes	0.0	0.0	0	--	0	--
	WBC		7.3		--		--
8686	Nucleated Red Cells	0		0		0	
	M. Neutrophils	75.0	6.3	0	--	0	--
	I. Neutrophils	0.0	0.0	0	--	0	--
	Lymphocytes	24.0	2.0	0	--	0	--
	Monocytes	1.0	0.1	0	--	0	--
	Eosinophils	0.0	0.0	0	--	0	--
	Basophils	0.0	0.0	0	--	0	--
	Atypical Lymphocytes	0.0	0.0	0	--	0	--
	Metamyelocytes	0.0	0.0	0	--	0	--
	WBC		8.4		--		--

WBC corrected for NRBC = or > 10

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18
STUDY NO: 193

GROUP: 2-M : 0.1 mg base/kg/day

SEX: MALE

Animal ID		WEEK 13		WEEK 18		WEEK 26	
		REL	ABS	REL	ABS	REL	ABS
8665	Nucleated Red Cells	0		0		0	
	M. Neutrophils	64.0	4.9	73.0	6.6	63.0	5.5
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	26.0	2.0	17.0	1.5	25.0	2.2
	Monocytes	5.0	0.4	4.0	0.4	5.0	0.4
	Eosinophils	5.0	0.4	6.0	0.5	7.0	0.6
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		7.7		9.1		8.7
8666	Nucleated Red Cells	0		0		0	
	M. Neutrophils	66.0	5.8	66.0	5.0	73.0	5.5
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	26.0	2.3	26.0	2.0	20.0	1.5
	Monocytes	5.0	0.4	1.0	0.1	3.0	0.2
	Eosinophils	3.0	0.3	7.0	0.5	4.0	0.3
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		8.8		7.5		7.5
8655	Nucleated Red Cells	0		0		0	
	M. Neutrophils	63.0	4.2	64.0	4.0	64.0	5.4
	I. Neutrophils	1.0	0.1	0.0	0.0	0.0	0.0
	Lymphocytes	31.0	2.1	29.0	1.8	28.0	2.4
	Monocytes	1.0	0.1	3.0	0.2	7.0	0.6
	Eosinophils	4.0	0.3	4.0	0.3	1.0	0.1
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		6.7		6.3		8.4

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18

STUDY NO: 193

GROUP: 2-M : 0.1 mg base/kg/day

SEX: MALE

Animal ID		WEEK 13		WEEK 18		WEEK 26	
		REL	ABS	REL	ABS	REL	ABS
8659	Nucleated Red Cells	0		0		0	
	M. Neutrophils	59.0	5.7	70.0	5.8	68.0	5.6
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	31.0	3.0	20.0	1.7	24.0	2.0
	Monocytes	6.0	0.6	3.0	0.2	5.0	0.4
	Eosinophils	4.0	0.4	7.0	0.6	3.0	0.2
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		9.6		8.3		8.2
8677	Nucleated Red Cells	0		0		0	
	M. Neutrophils	73.0	6.6	0	--	0	--
	I. Neutrophils	0.0	0.0	0	--	0	--
	Lymphocytes	25.0	2.3	0	--	0	--
	Monocytes	1.0	0.1	0	--	0	--
	Eosinophils	1.0	0.1	0	--	0	--
	Basophils	0.0	0.0	0	--	0	--
	Atypical Lymphocytes	0.0	0.0	0	--	0	--
	Metamyelocytes	0.0	0.0	0	--	0	--
	WBC		9.0		--		--

WBC corrected for NRBC = or > 10

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18

STUDY NO: 193

GROUP: 3-M : 0.3 mg base/kg/day

SEX: MALE

Animal ID		WEEK 13		WEEK 18		WEEK 26	
		REL	ABS	REL	ABS	REL	ABS
8668	Nucleated Red Cells	0		0		0	
	M. Neutrophils	67.0	7.2	0	--	0	--
	I. Neutrophils	0.0	0.0	0	--	0	--
	Lymphocytes	21.0	2.3	0	--	0	--
	Monocytes	8.0	0.9	0	--	0	--
	Eosinophils	4.0	0.4	0	--	0	--
	Basophils	0.0	0.0	0	--	0	--
	Atypical Lymphocytes	0.0	0.0	0	--	0	--
	Metamyelocytes	0.0	0.0	0	--	0	--
	WBC		10.8		--		--
8682	Nucleated Red Cells	0		0		0	
	M. Neutrophils	76.0	4.9	70.0	3.4	71.0	2.9
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	18.0	1.2	20.0	1.0	21.0	0.9
	Monocytes	4.0	0.3	5.0	0.2	2.0	0.1
	Eosinophils	2.0	0.1	5.0	0.2	6.0	0.2
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		6.5		4.9		4.1
8684	Nucleated Red Cells	0		0		0	
	M. Neutrophils	72.0	7.6	0	--	0	--
	I. Neutrophils	0.0	0.0	0	--	0	--
	Lymphocytes	19.0	2.0	0	--	0	--
	Monocytes	3.0	0.3	0	--	0	--
	Eosinophils	6.0	0.6	0	--	0	--
	Basophils	0.0	0.0	0	--	0	--
	Atypical Lymphocytes	0.0	0.0	0	--	0	--
	Metamyelocytes	0.0	0.0	0	--	0	--
	WBC		10.6		--		--

WBC corrected for NRBC = or > 10

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18

STUDY NO: 193

GROUP: 3-M : 0.3 mg base/kg/day

SEX: MALE

Animal ID		WEEK 13		WEEK 18		WEEK 26	
		REL	ABS	REL	ABS	REL	ABS
8674	Nucleated Red Cells	0		0		0	
	M. Neutrophils	64.0	4.9	64.0	4.5	67.0	5.0
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	31.0	2.4	29.0	2.0	28.0	2.1
	Monocytes	4.0	0.3	6.0	0.4	2.0	0.2
	Eosinophils	1.0	0.1	1.0	0.1	3.0	0.2
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		7.7		7.0		7.5
8653	Nucleated Red Cells	0		0		0	
	M. Neutrophils	84.0	7.1	0	--	0	--
	I. Neutrophils	0.0	0.0	0	--	0	--
	Lymphocytes	13.0	1.1	0	--	0	--
	Monocytes	2.0	0.2	0	--	0	--
	Eosinophils	1.0	0.1	0	--	0	--
	Basophils	0.0	0.0	0	--	0	--
	Atypical Lymphocytes	0.0	0.0	0	--	0	--
	Metamyelocytes	0.0	0.0	0	--	0	--
	WBC		8.4		--		--
8660	Nucleated Red Cells	0		0		0	
	M. Neutrophils	70.0	6.9	0	--	0	--
	I. Neutrophils	0.0	0.0	0	--	0	--
	Lymphocytes	24.0	2.4	0	--	0	--
	Monocytes	4.0	0.4	0	--	0	--
	Eosinophils	2.0	0.2	0	--	0	--
	Basophils	0.0	0.0	0	--	0	--
	Atypical Lymphocytes	0.0	0.0	0	--	0	--
	Metamyelocytes	0.0	0.0	0	--	0	--
	WBC		9.8		--		--

WBC corrected for NRBC = or > 10

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18
STUDY NO: 193

GROUP: 3-M : 0.3 mg base/kg/day

SEX: MALE

Animal ID		WEEK 13		WEEK 18		WEEK 26	
		REL	ABS	REL	ABS	REL	ABS
8662	Nucleated Red Cells	1		0		0	
	M. Neutrophils	70.0	6.3	80.0	5.5	62.0	4.7
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	22.0	2.0	10.0	0.7	35.0	2.6
	Monocytes	3.0	0.3	6.0	0.4	0.0	0.0
	Eosinophils	5.0	0.5	4.0	0.3	3.0	0.2
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		9.0		6.9		7.5
8688	Nucleated Red Cells	0		0		0	
	M. Neutrophils	50.0	3.4	60.0	4.1	64.0	3.7
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	45.0	3.0	29.0	2.0	32.0	1.9
	Monocytes	4.0	0.3	2.0	0.1	2.0	0.1
	Eosinophils	1.0	0.1	9.0	0.6	2.0	0.1
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		6.7		6.9		5.8

WBC corrected for NRBC = or > 10

(--) - Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18

STUDY NO: 193

GROUP: 4-M : 1.0 mg base/kg/day

SEX: MALE

Animal ID		WEEK 13		WEEK 18		WEEK 26	
		REL	ABS	REL	ABS	REL	ABS
8661	Nucleated Red Cells	0		0		0	
	M. Neutrophils	57.0	5.4	0	--	0	--
	I. Neutrophils	0.0	0.0	0	--	0	--
	Lymphocytes	34.0	3.2	0	--	0	--
	Monocytes	3.0	0.3	0	--	0	--
	Eosinophils	6.0	0.6	0	--	0	--
	Basophils	0.0	0.0	0	--	0	--
	Atypical Lymphocytes	0.0	0.0	0	--	0	--
	Metamyelocytes	0.0	0.0	0	--	0	--
	WBC		9.4		--		--
8670	Nucleated Red Cells	0		0		0	
	M. Neutrophils	80.0	11.4	0	--	0	--
	I. Neutrophils	0.0	0.0	0	--	0	--
	Lymphocytes	13.0	1.9	0	--	0	--
	Monocytes	7.0	1.0	0	--	0	--
	Eosinophils	0.0	0.0	0	--	0	--
	Basophils	0.0	0.0	0	--	0	--
	Atypical Lymphocytes	0.0	0.0	0	--	0	--
	Metamyelocytes	0.0	0.0	0	--	0	--
	WBC		14.3		--		--
8681	Nucleated Red Cells	0		0		0	
	M. Neutrophils	74.0	8.2	0	--	0	--
	I. Neutrophils	0.0	0.0	0	--	0	--
	Lymphocytes	18.0	2.0	0	--	0	--
	Monocytes	4.0	0.4	0	--	0	--
	Eosinophils	4.0	0.4	0	--	0	--
	Basophils	0.0	0.0	0	--	0	--
	Atypical Lymphocytes	0.0	0.0	0	--	0	--
	Metamyelocytes	0.0	0.0	0	--	0	--
	WBC		11.1		--		--

WBC corrected for NRBC = or > 10

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18

STUDY NO: 193

GROUP: 4-M : 1.0 mg base/kg/day

SEX: MALE

Animal ID		WEEK 13		WEEK 18		WEEK 26	
		REL	ABS	REL	ABS	REL	ABS
8664	Nucleated Red Cells	0		0		0	
	M. Neutrophils	67.0	6.4	0	--	0	--
	I. Neutrophils	0.0	0.0	0	--	0	--
	Lymphocytes	26.0	2.5	0	--	0	--
	Monocytes	7.0	0.7	0	--	0	--
	Eosinophils	0.0	0.0	0	--	0	--
	Basophils	0.0	0.0	0	--	0	--
	Atypical Lymphocytes	0.0	0.0	0	--	0	--
	Metamyelocytes	0.0	0.0	0	--	0	--
	WBC		9.6		--		--
8675	Nucleated Red Cells	0		0		0	
	M. Neutrophils	75.0	5.8	51.0	2.8	67.0	4.6
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	18.0	1.4	40.0	2.2	25.0	1.7
	Monocytes	2.0	0.2	5.0	0.3	3.0	0.2
	Eosinophils	5.0	0.4	4.0	0.2	5.0	0.3
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		7.7		5.5		6.8
8683	Nucleated Red Cells	0		0		0	
	M. Neutrophils	76.0	11.0	58.0	3.3	66.0	5.3
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	19.0	2.8	33.0	1.9	30.0	2.4
	Monocytes	4.0	0.6	6.0	0.3	0.0	0.0
	Eosinophils	1.0	0.1	3.0	0.2	4.0	0.3
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		14.5		5.7		8.1

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18

STUDY NO: 193

GROUP: 4-M : 1.0 mg base/kg/day

SEX: MALE

Animal ID		WEEK 13		WEEK 18		WEEK 26	
		REL	ABS	REL	ABS	REL	ABS
8658	Nucleated Red Cells	0		0		0	
	M. Neutrophils	66.0	6.1	85.0	7.7	64.0	4.7
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	21.0	2.0	10.0	0.9	31.0	2.3
	Monocytes	7.0	0.7	4.0	0.4	1.0	0.1
	Eosinophils	6.0	0.6	1.0	0.1	4.0	0.3
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		9.3		9.0		7.3
8652	Nucleated Red Cells	0		0		0	
	M. Neutrophils	71.0	16.8	61.0	6.9	68.0	9.3
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	19.0	4.5	28.0	3.2	22.0	3.0
	Monocytes	4.0	0.9	2.0	0.2	4.0	0.5
	Eosinophils	6.0	1.4	9.0	1.0	6.0	0.8
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		23.7		11.3		13.7

WBC corrected for NRBC = or > 10

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: UIC-18
STUDY NO: 193

GROUP: 1-M : 0 mg base/kg/day

SEX: MALE

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8
8656	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	Anisocytosis,Slight; Clumped Platelets, Slight
8687	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
8669	Normal Red Blood Cells	Normal Red Blood Cells	Clumped Platelets, Slight	Normal Red Blood Cells
8673	Normal Red Blood Cells	Normal Red Blood Cells	Clumped Platelets, Slight	Normal Red Blood Cells
8667	Normal Red Blood Cells	Poikilocytes,Slight	Normal Red Blood Cells	Normal Red Blood Cells
8654	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
8680	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
8676	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: UIC-18

SEX: MALE

STUDY NO: 193

GROUP: 2-M : 0.1 mg base/kg/day

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8
8685	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
8663	Normal Red Blood Cells	Normal Red Blood Cells	Anisocytosis,Slight	Normal Red Blood Cells
8686	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	Anisocytosis,Slight
8665	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
8666	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells;Clumped Platelets,Slight	Normal Red Blood Cells
8655	Normal Red Blood Cells	Normal Red Blood Cells	Anisocytosis,Slight	Normal Red Blood Cells
8659	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
8677	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: UIC-18
STUDY NO: 193

GROUP: 3-M : 0.3 mg base/kg/day

SEX: MALE

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8
8674	Normal Red Blood Cells	Polychromasia,Slight	Anisocytosis,Slight	Anisocytosis,Slight
8653	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
8660	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
8668	Normal Red Blood Cells	Anisocytosis,Slight	Normal Red Blood Cells	Normal Red Blood Cells
8682	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	Clumped Platelets, Slight;Normal Red Blood Cells
8684	Normal Red Blood Cells;Clumped Platelets,Slight	Normal Red Blood Cells	Normal Red Blood Cells;Large Platelets,Slight	Anisocytosis,Slight
8662	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells;Clumped Platelets,Slight	Normal Red Blood Cells
8688	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	Anisocytosis,Slight

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: UIC-18

SEX: MALE

STUDY NO: 193

GROUP: 4-M : 1.0 mg base/kg/day

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8
8661	Normal Red Blood Cells	Normal Red Blood Cells	Large Platelets	Normal Red Blood Cells
8670	Normal Red Blood Cells	Normal Red Blood Cells	Large Platelets, Slight	Anisocytosis, Slight
8681	Normal Red Blood Cells	Normal Red Blood Cells	Large Platelets, Slight	Large Platelets, Slight; Normal Red Blood Cells
8664	Normal Red Blood Cells	Normal Red Blood Cells	Large Platelets, Slight	Anisocytosis, Slight
8675	Normal Red Blood Cells	Normal Red Blood Cells	Large Platelets, Slight; Polychromasia Slight; Anisocytosis, Slight	Normal Red Blood Cells
8683	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	Anisocytosis, Slight
8658	Normal Red Blood Cells	Normal Red Blood Cells	Clumped Platelets, Slight	Normal Red Blood Cells
8652	Normal Red Blood Cells	Normal Red Blood Cells	Large Platelets, Slight; Polychromasia Slight	Clumped Platelets, Slight; Normal Red Blood Cells

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: UIC-18
STUDY NO: 193

GROUP: 1-M : 0 mg base/kg/day

SEX: MALE

Animal ID	WEEK 13	WEEK 18	WEEK 26
8656	Anisocytosis,Slight	--	--
8687	Normal Red Blood Cells	--	--
8669	Normal Red Blood Cells	--	--
8673	Normal Red Blood Cells	--	--
8667	Normal Red Blood Cells;Clumped Platelets,Slight	Normal Red Blood Cells	Normal Red Blood Cells
8654	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells;Clumped Platelets,Slight
8680	Normal Red Blood Cells	Normal Red Blood Cells;Clumped Platelets	Normal Red Blood Cells
8676	Anisocytosis,Slight	Large Platelets; Anisocytosis,Slight	Normal Red Blood Cells

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: UIC-18
STUDY NO: 193

GROUP: 2-M : 0.1 mg base/kg/day

SEX: MALE

Animal ID	WEEK 13	WEEK 18	WEEK 26
8685	Normal Red Blood Cells	--	--
8663	Normal Red Blood Cells	--	--
8686	Anisocytosis,Slight	--	--
8665	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
8666	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
8655	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
8659	Normal Red Blood Cells	Normal Red Blood Cells	Anisocytosis,Slight
8677	Anisocytosis,Slight	--	--

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: UIC-18
STUDY NO: 193

GROUP: 3-M : 0.3 mg base/kg/day

SEX: MALE

Animal ID	WEEK 13	WEEK 18	WEEK 26
8674	Normal Red Blood Cells	Anisocytosis,Slight	Normal Red Blood Cells
8653	Normal Red Blood Cells	--	--
8660	Normal Red Blood Cells	--	--
8668	Normal Red Blood Cells	--	--
8682	Normal Red Blood Cells	Normal Red Blood Cells	Anisocytosis,Slight
8684	Normal Red Blood Cells	--	--
8662	Normal Red Blood Cells	Normal Red Blood Cells;Large Platelets	Normal Red Blood Cells
8688	Normal Red Blood Cells	Poikilocytes,Slight	Clumped Platelets, Slight

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: UIC-18
STUDY NO: 193

GROUP: 4-M : 1.0 mg base/kg/day

SEX: MALE

Animal ID	WEEK 13	WEEK 18	WEEK 26
8661	Normal Red Blood Cells;Large Platelets,Slight	--	--
8670	Normal Red Blood Cells	--	--
8681	Normal Red Blood Cells	--	--
8664	Normal Red Blood Cells;Clumped Platelets,Slight	--	--
8675	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
8683	Normal Red Blood Cells	Normal Red Blood Cells	Clumped Platelets, Slight
8658	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
8652	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Erythrocytes

STUDY ID: UIC-18
STUDY NO: 193
ABBR: RBC

SEX: FEMALE

UNITS: $10^6/\text{mm}^3$

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
GROUP: 1-F:0 mg base/kg/day							
8721	5.95	6.09	7.01	6.99	6.44	--	--
8712	6.63	6.57	6.21	5.91	6.26	--	--
8710	6.19	6.05	6.54	6.48	6.71	--	--
8723	7.08	6.70	7.50	7.11	5.97	--	--
8705	6.79	6.11	6.44	6.21	6.68	6.63	6.43
8700	6.88	6.13	7.21	6.63	6.83	7.00	6.16
8699	6.30	6.50	7.70	7.66	6.78	6.34	6.99
8690	6.77	5.65	6.11	5.52	6.35	6.64	6.38
MEAN	6.57	6.23	6.84	6.56	6.50	6.65	6.49
SD	0.387	0.343	0.600	0.690	0.300	0.270	0.353
N	8	8	8	8	8	4	4

GROUP: 2-F:0.1 mg base/kg/day							
8717	6.86	6.13	5.98	5.98	5.85	--	--
8703	6.85	6.95	7.44	6.61	7.06	--	--
8713	6.78	7.13	6.50	5.88	6.86	--	--
8693	6.77	6.40	6.63	6.21	6.59	--	--
8695	7.40	7.65	7.09	7.56	8.14	7.20	7.37
8709	6.58	6.79	6.34	6.33	7.18	6.69	6.87
8715	7.04	6.59	6.71	6.66	7.18	7.66	7.57
8697	6.66	6.41	6.63	6.87	7.21	6.94	7.06
MEAN	6.87	6.76	6.67	6.51	7.01	7.12	7.22
SD	0.255	0.485	0.445	0.543	0.646	0.414	0.313
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Erythrocytes

STUDY ID: UIC-18

SEX: FEMALE

STUDY NO: 193

ABBR: RBC

UNITS: $10^6/\text{mm}^3$

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
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GROUP: 3-F:0.3 mg base/kg/day

8692	6.43	6.18	6.28	5.86	5.37	--	--
8718	6.73	6.27	6.15	5.75	6.58	--	--
8706	6.12	5.98	5.51	6.12	6.38	--	--
8714	6.54	6.08	5.98	6.62	6.90	--	--
8701	7.02	7.19	7.59	6.87	7.41	7.29	7.62
8702	6.92	7.09	6.80	6.54	6.43	6.61	7.01
8720	6.37	6.11	6.19	6.23	6.47	5.92	6.18
8704	6.04	6.08	5.93	6.64	6.00	5.48	7.11

MEAN	6.52	6.37	6.30	6.33	6.44	6.33	6.98
SD	0.354	0.482	0.634	0.401	0.599	0.794	0.596
N	8	8	8	8	8	4	4

GROUP: 4-F:1.0 mg base/kg/day

8696	6.94	7.07	6.35	6.62	7.36	--	--
8719	6.32	5.66	5.81	6.09	6.56	--	--
8711	6.94	6.80	6.11	6.51	7.07	--	--
8716	6.36	7.35	6.23	6.90	7.00	--	--
8725	7.20	7.34	6.26	7.21	6.70	6.02	5.84
8707	6.47	6.66	6.00	6.29	7.22	7.13	6.82
8689	7.12	6.82	5.87	7.01	6.50	6.56	7.09
8722	6.21	6.51	6.27	6.25	7.13	5.78	6.47

MEAN	6.70	6.78	6.11	6.61	6.94	6.37	6.56
SD	0.395	0.543	0.200	0.399	0.318	0.601	0.540
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

D R A F T

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Hemoglobin

STUDY ID: UIC-18
STUDY NO: 193
ABBR: HGB

SEX: FEMALE

UNITS: g/dL

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
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GROUP: 1-F:0 mg base/kg/day

8721	14.6	14.9	16.7	16.9	15.1	--	--
8712	16.3	16.0	15.5	14.8	15.4	--	--
8710	15.1	14.9	16.1	16.1	16.4	--	--
8723	17.6	16.6	18.5	17.5	14.6	--	--
8705	17.2	15.5	16.4	15.5	16.8	16.6	16.2
8700	16.8	15.1	17.5	16.3	16.7	16.8	14.9
8699	15.8	16.1	19.0	19.2	17.1	15.5	17.4
8690	17.0	14.2	15.2	13.9	15.6	16.4	15.4
MEAN	16.3	15.4	16.9	16.3	16.0	16.3	16.0
SD	1.06	0.79	1.37	1.64	0.91	0.57	1.09
N	8	8	8	8	8	4	4

GROUP: 2-F:0.1 mg base/kg/day

8717	16.9	15.0	14.7	15.2	14.5	--	--
8703	17.1	16.7	18.2	16.2	17.1	--	--
8713	15.5	16.5	15.7	14.4	16.2	--	--
8693	16.6	15.6	16.2	15.1	15.7	--	--
8695	17.9	18.4	17.3	18.7	19.8	17.3	17.8
8709	16.1	16.6	15.6	15.6	17.5	16.0	16.4
8715	17.2	15.8	15.8	16.2	16.9	17.8	17.6
8697	16.5	15.6	16.2	17.0	17.8	17.0	17.3
MEAN	16.7	16.3	16.2	16.1	16.9	17.0	17.3
SD	0.73	1.04	1.08	1.34	1.57	0.76	0.62
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Hemoglobin

STUDY ID: UIC-18
STUDY NO: 193
ABBR: HGB

SEX: FEMALE

UNITS: g/dL

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
GROUP: 3-F:0.3 mg base/kg/day							
8692	15.3	14.8	15.2	14.1	12.8	--	--
8718	16.1	14.9	14.7	13.9	15.6	--	--
8706	15.1	14.7	14.0	15.3	15.7	--	--
8714	15.2	14.5	14.7	16.4	16.6	--	--
8701	16.6	16.4	17.9	16.3	17.3	16.7	18.0
8702	16.3	16.5	16.1	15.1	14.6	15.0	15.9
8720	15.5	15.0	15.2	15.6	16.0	14.3	15.0
8704	14.8	14.6	14.7	16.5	14.5	12.9	16.7
MEAN	15.6	15.2	15.3	15.4	15.4	14.7	16.4
SD	0.64	0.80	1.21	1.01	1.40	1.58	1.27
N	8	8	8	8	8	4	4

GROUP: 4-F:1.0 mg base/kg/day							
8696	17.0	17.7	16.1	16.8	18.6	--	--
8719	15.2	13.7	14.1	14.4	15.1	--	--
8711	16.6	16.2	14.5	14.7	16.0	--	--
8716	15.4	17.4	15.5	16.3	16.8	--	--
8725	17.0	17.6	15.2	16.7	15.5	14.0	13.2
8707	16.6	16.5	15.4	15.2	17.6	17.2	16.2
8689	17.7	16.5	15.0	16.9	16.0	15.5	16.6
8722	16.0	16.4	15.9	15.4	17.3	14.4	16.0
MEAN	16.4	16.5	15.2	15.8	16.6	15.3	15.5
SD	0.85	1.28	0.67	1.00	1.18	1.43	1.55
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Hematocrit

STUDY ID: UIC-18
STUDY NO: 193
ABBR: HCT

SEX: FEMALE

UNITS: %

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
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GROUP: 1-F:0 mg base/kg/day

8721	41.3	42.1	48.6	47.6	44.9	--	--
8712	46.3	45.6	43.3	41.2	44.4	--	--
8710	43.6	42.5	45.7	45.3	48.3	--	--
8723	49.7	46.6	52.4	49.7	42.1	--	--
8705	50.2	45.0	47.5	45.6	49.5	49.1	47.8
8700	48.2	42.8	50.3	45.9	48.4	48.7	43.1
8699	44.5	45.6	54.3	53.7	48.9	45.0	49.8
8690	48.9	40.7	43.7	39.0	46.1	48.3	45.1

MEAN	46.6	43.9	48.2	46.0	46.6	47.8	46.5
SD	3.21	2.10	3.97	4.60	2.62	1.88	2.95
N	8	8	8	8	8	4	4

GROUP: 2-F:0.1 mg base/kg/day

8717	48.2	42.5	42.3	42.8	41.7	--	--
8703	48.6	48.9	52.4	46.5	49.9	--	--
8713	46.6	49.0	45.0	41.1	48.6	--	--
8693	47.2	44.5	46.4	43.3	46.2	--	--
8695	50.8	52.6	48.9	52.5	56.9	49.1	52.1
8709	46.8	47.8	45.1	44.9	51.2	47.1	48.7
8715	47.4	44.2	45.0	44.6	48.8	51.4	50.5
8697	47.4	45.3	47.9	49.3	52.6	49.8	50.4

MEAN	47.9	46.9	46.6	45.6	49.5	49.4	50.4
SD	1.36	3.31	3.08	3.72	4.48	1.78	1.39
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Hematocrit

STUDY ID: UIC-18
STUDY NO: 193
ABBR: HCT

SEX: FEMALE

UNITS: %

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
GROUP: 3-F:0.3 mg base/kg/day							
8692	44.7	42.6	43.8	40.8	37.2	--	--
8718	46.6	43.0	43.4	40.4	46.3	--	--
8706	43.3	42.0	40.4	44.6	45.9	--	--
8714	45.6	42.3	43.1	47.4	50.5	--	--
8701	47.9	48.3	51.8	47.9	50.6	48.8	51.4
8702	46.3	47.4	45.9	43.7	42.5	43.1	45.8
8720	44.6	42.6	44.3	45.0	47.0	41.7	43.6
8704	42.5	42.8	42.8	46.6	42.4	38.0	48.8
MEAN	45.2	43.9	44.4	44.6	45.3	42.9	47.4
SD	1.78	2.48	3.35	2.82	4.49	4.48	3.41
N	8	8	8	8	8	4	4

GROUP: 4-F:1.0 mg base/kg/day							
8696	49.5	50.1	46.9	47.7	54.4	--	--
8719	43.7	39.1	41.2	40.4	44.5	--	--
8711	47.7	46.6	43.1	42.5	46.9	--	--
8716	45.0	51.6	46.2	49.0	50.5	--	--
8725	50.4	50.4	44.9	49.7	46.9	41.8	39.2
8707	46.2	47.2	45.2	44.3	51.9	50.3	47.3
8689	50.1	47.9	43.7	49.6	46.9	47.2	48.4
8722	45.3	47.2	46.3	44.3	50.5	42.0	46.0
MEAN	47.2	47.5	44.7	45.9	49.1	45.3	45.2
SD	2.56	3.85	1.92	3.54	3.28	4.15	4.13
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Mean Corpuscular Volume

STUDY ID: UIC-18
STUDY NO: 193
ABBR: MCV

SEX: FEMALE

UNITS: fL

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
GROUP: 1-F:0 mg base/kg/day							
8721	69.4	69.1	69.3	68.1	69.7	--	--
8712	69.8	69.4	69.7	69.7	70.9	--	--
8710	70.4	70.2	69.9	69.9	72.0	--	--
8723	70.2	69.6	69.9	69.9	70.5	--	--
8705	73.9	73.6	73.8	73.4	74.1	74.1	74.3
8700	70.1	69.8	69.8	69.2	70.9	69.6	70.0
8699	70.6	70.2	70.5	70.1	72.1	71.0	71.2
8690	72.2	72.0	71.5	70.7	72.6	72.7	70.7
MEAN	70.8	70.5	70.6	70.1	71.6	71.9	71.6
SD	1.49	1.54	1.47	1.53	1.39	1.96	1.90
N	8	8	8	8	8	4	4

GROUP: 2-F:0.1 mg base/kg/day							
8717	70.3	69.3	70.7	71.6	71.3	--	--
8703	70.9	70.4	70.4	70.3	70.7	--	--
8713	68.7	68.7	69.2	69.9	70.8	--	--
8693	69.7	69.5	70.0	69.7	70.1	--	--
8695	68.6	68.8	69.0	69.4	69.9	68.2	70.7
8709	71.1	70.4	71.1	70.9	71.3	70.4	70.9
8715	67.3	67.1	67.1	67.0	68.0	67.1	66.7
8697	71.2	70.7	72.2	71.8	73.0	71.8	71.4
MEAN	69.7	69.4	70.0	70.1	70.6	69.4	69.9
SD	1.41	1.19	1.55	1.52	1.43	2.12	2.17
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Mean Corpuscular Volume

STUDY ID: UIC-18
STUDY NO: 193
ABBR: MCV

SEX: FEMALE

UNITS: fL

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
GROUP: 3-F:0.3 mg base/kg/day							
8692	69.5	68.9	69.7	69.6	69.3	--	--
8718	69.2	68.6	70.6	70.3	70.4	--	--
8706	70.8	70.2	73.3	72.9	71.9	--	--
8714	69.7	69.6	72.1	71.6	73.2	--	--
8701	68.2	67.2	68.2	69.7	68.3	66.9	67.5
8702	66.9	66.9	67.5	66.8	66.1	65.2	65.3
8720	70.0	69.7	71.6	72.2	72.6	70.4	70.6
8704	70.4	70.4	72.2	70.2	70.7	69.3	68.6
MEAN	69.3	68.9	70.6	70.4	70.3	68.0	68.0
SD	1.26	1.31	2.04	1.89	2.36	2.34	2.21
N	8	8	8	8	8	4	4

GROUP: 4-F:1.0 mg base/kg/day							
8696	71.3	70.9	73.9	72.1	73.9	--	--
8719	69.1	69.1	70.9	66.3	67.8	--	--
8711	68.7	68.5	70.5	65.3	66.3	--	--
8716	70.8	70.2	74.2	71.0	72.1	--	--
8725	70.0	68.7	71.7	68.9	70.0	69.4	67.1
8707	71.4	70.9	75.3	70.4	71.9	70.5	69.4
8689	70.4	70.2	74.4	70.8	72.2	72.0	68.3
8722	72.9	72.5	73.8	70.9	70.8	72.7	71.1
MEAN	70.6	70.1	73.1	69.5	70.6	71.1	69.0
SD	1.35	1.34	1.79	2.44	2.51	1.48	1.70
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Mean Corpuscular Hemo.

STUDY ID: UIC-18
STUDY NO: 193
ABBR: MCH

SEX: FEMALE

UNITS: pg

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
GROUP: 1-F:0 mg base/kg/day							
8721	24.5	24.5	23.8	24.2	23.4	--	--
8712	24.6	24.4	25.0	25.0	24.6	--	--
8710	24.4	24.6	24.6	24.8	24.4	--	--
8723	24.9	24.8	24.7	24.6	24.5	--	--
8705	25.3	25.4	25.5	25.0	25.1	25.0	25.2
8700	24.4	24.6	24.3	24.6	24.5	24.0	24.2
8699	25.1	24.8	24.7	25.1	25.2	24.4	24.9
8690	25.1	26.1	24.9	25.2	24.6	24.7	24.1
MEAN	24.8	24.9	24.7	24.8	24.5	24.5	24.6
SD	0.36	0.57	0.50	0.33	0.54	0.43	0.54
N	8	8	8	8	8	4	4

GROUP: 2-F:0.1 mg base/kg/day							
8717	24.6	24.5	24.6	25.4	24.8	--	--
8703	25.0	24.0	24.5	24.5	24.2	--	--
8713	22.9	23.1	24.2	24.5	23.6	--	--
8693	24.5	24.4	24.4	24.3	23.8	--	--
8695	24.2	24.1	24.4	24.7	24.3	24.0	24.2
8709	24.5	24.4	24.6	24.6	24.4	23.9	23.9
8715	24.4	24.0	23.5	24.3	23.5	23.2	23.2
8697	24.8	24.3	24.4	24.7	24.7	24.5	24.5
MEAN	24.4	24.1	24.3	24.6	24.2	23.9	24.0
SD	0.64	0.45	0.36	0.35	0.49	0.54	0.56
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Mean Corpuscular Hemo.

STUDY ID: UIC-18

SEX: FEMALE

STUDY NO: 193

ABBR: MCH

UNITS: pg

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
GROUP: 3-F:0.3 mg base/kg/day							
8692	23.8	23.9	24.2	24.1	23.8	--	--
8718	23.9	23.8	23.9	24.2	23.7	--	--
8706	24.7	24.6	25.4	25.0	24.6	--	--
8714	23.2	23.8	24.6	24.8	24.1	--	--
8701	23.6	22.8	23.6	23.7	23.3	22.9	23.6
8702	23.6	23.3	23.7	23.1	22.7	22.7	22.7
8720	24.3	24.5	24.6	25.0	24.7	24.2	24.3
8704	24.5	24.0	24.8	24.8	24.2	23.5	23.5
MEAN	24.0	23.8	24.4	24.3	23.9	23.3	23.5
SD	0.51	0.59	0.61	0.69	0.67	0.68	0.66
N	8	8	8	8	8	4	4

GROUP: 4-F:1.0 mg base/kg/day							
8696	24.5	25.0	25.4	25.4	25.3	--	--
8719	24.1	24.2	24.3	23.6	23.0	--	--
8711	23.9	23.8	23.7	22.6	22.6	--	--
8716	24.2	23.7	24.9	23.6	24.0	--	--
8725	23.6	24.0	24.3	23.2	23.1	23.3	22.6
8707	25.7	24.8	25.7	24.2	24.4	24.1	23.8
8689	24.9	24.2	25.6	24.1	24.6	23.6	23.4
8722	25.8	25.2	25.4	24.6	24.3	24.9	24.7
MEAN	24.6	24.4	24.9	23.9	23.9	24.0	23.6
SD	0.81	0.57	0.74	0.86	0.93	0.70	0.87
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Mean Corpus. Hemo. Conc.

STUDY ID: UIC-18
STUDY NO: 193
ABBR: MCHC

SEX: FEMALE

UNITS: g/dL

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
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GROUP: 1-F:0 mg base/kg/day

8721	35.4	35.4	34.4	35.5	33.6	--	--
8712	35.2	35.1	35.8	35.9	34.7	--	--
8710	34.6	35.1	35.2	35.5	34.0	--	--
8723	35.4	35.6	35.3	35.2	34.7	--	--
8705	34.3	34.4	34.5	34.0	33.9	33.8	33.9
8700	34.9	35.3	34.8	35.5	34.5	34.5	34.6
8699	35.5	35.3	35.0	35.8	35.0	34.4	34.9
8690	34.8	34.9	34.8	35.6	33.8	34.0	34.1
MEAN	35.0	35.1	35.0	35.4	34.3	34.2	34.4
SD	0.43	0.37	0.46	0.59	0.51	0.33	0.46
N	8	8	8	8	8	4	4

GROUP: 2-F:0.1 mg base/kg/day

8717	35.1	35.3	34.8	35.5	34.8	--	--
8703	35.2	34.2	34.7	34.8	34.3	--	--
8713	33.3	33.7	34.9	35.0	33.3	--	--
8693	35.2	35.1	34.9	34.9	34.0	--	--
8695	35.2	35.0	35.4	35.6	34.8	35.2	34.2
8709	34.4	34.7	34.6	34.7	34.2	34.0	33.7
8715	36.3	35.7	35.1	36.3	34.6	34.6	34.9
8697	34.8	34.4	33.8	34.5	33.8	34.1	34.3
MEAN	34.9	34.8	34.8	35.2	34.2	34.5	34.3
SD	0.85	0.65	0.47	0.60	0.52	0.55	0.49
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Mean Corpus. Hemo. Conc.

STUDY ID: UIC-18

SEX: FEMALE

STUDY NO: 193

ABBR: MCHC

UNITS: g/dL

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
GROUP: 3-F:0.3 mg base/kg/day							
8692	34.2	34.7	34.7	34.6	34.4	--	--
8718	34.5	34.7	33.9	34.4	33.7	--	--
8706	34.9	35.0	34.7	34.3	34.2	--	--
8714	33.3	34.3	34.1	34.6	32.9	--	--
8701	34.7	34.0	34.6	34.0	34.2	34.2	35.0
8702	35.2	34.8	35.1	34.6	34.4	34.8	34.7
8720	34.8	35.2	34.3	34.7	34.0	34.3	34.4
8704	34.8	34.1	34.3	35.4	34.2	33.9	34.2
MEAN	34.6	34.6	34.5	34.6	34.0	34.3	34.6
SD	0.58	0.43	0.39	0.40	0.50	0.37	0.35
N	8	8	8	8	8	4	4

GROUP: 4-F:1.0 mg base/kg/day							
8696	34.3	35.3	34.3	35.2	34.2	--	--
8719	34.8	35.0	34.2	35.6	33.9	--	--
8711	34.8	34.8	33.6	34.6	34.1	--	--
8716	34.2	33.7	33.5	33.3	33.3	--	--
8725	33.7	34.9	33.9	33.6	33.0	33.5	33.7
8707	35.9	35.0	34.1	34.3	33.9	34.2	34.2
8689	35.3	34.4	34.3	34.1	34.1	32.8	34.3
8722	35.3	34.7	34.3	34.8	34.3	34.3	34.8
MEAN	34.8	34.7	34.0	34.4	33.9	33.7	34.3
SD	0.71	0.49	0.32	0.78	0.46	0.70	0.45
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Reticulocytes

STUDY ID: UIC-18

SEX: FEMALE

STUDY NO: 193

ABBR: RETICS

UNITS: % RBCs

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
GROUP: 1-F:0 mg base/kg/day							
8721	0.4	0.9	0.3	0.8	0.3	--	--
8712	0.1	0.5	0.3	0.5	1.0	--	--
8710	0.3	0.3	0.4	0.2	0.0	--	--
8723	0.0	0.4	0.6	0.2	0.2	--	--
8705	0.3	0.4	0.2	0.3	0.3	0.3	0.1
8700	0.3	0.1	0.4	0.3	0.4	0.4	0.2
8699	0.3	0.0	0.6	0.3	0.4	0.2	0.3
8690	0.2	0.2	0.2	0.3	0.6	0.2	0.1
MEAN	0.2	0.4	0.4	0.4	0.4	0.3	0.2
SD	0.13	0.28	0.16	0.20	0.30	0.10	0.10
N	8	8	8	8	8	4	4
GROUP: 2-F:0.1 mg base/kg/day							
8717	0.2	0.1	0.3	0.3	0.3	--	--
8703	0.0	0.5	0.4	0.1	0.1	--	--
8713	0.2	0.4	0.2	0.4	0.2	--	--
8693	0.8	0.2	0.0	0.3	0.3	--	--
8695	0.0	0.0	0.5	0.5	0.3	0.5	0.8
8709	0.4	0.3	0.5	0.3	0.7	0.4	1.0
8715	0.5	0.1	0.7	0.2	0.5	0.3	0.3
8697	0.3	0.1	0.4	0.8	0.1	0.5	0.4
MEAN	0.3	0.2	0.4	0.4	0.3	0.4	0.6
SD	0.27	0.17	0.21	0.21	0.20	0.10	0.33
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Reticulocytes

STUDY ID: UIC-18

SEX: FEMALE

STUDY NO: 193

ABBR: RETICS

UNITS: % RBCs

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
GROUP: 3-F:0.3 mg base/kg/day							
8692	0.5	0.5	0.6	0.5	0.3	--	--
8718	0.2	0.1	0.6	0.7	0.3	--	--
8706	0.0	0.3	0.8	1.4	0.8	--	--
8714	0.0	0.2	0.7	0.4	0.5	--	--
8701	0.1	0.2	0.3	0.8	0.3	0.6	0.3
8702	0.2	0.8	0.6	0.9	0.6	0.9	0.5
8720	0.3	0.4	0.4	0.5	0.3	0.0	0.2
8704	0.0	0.4	0.8	0.4	0.5	0.0	0.4
MEAN	0.2	0.4	0.6	0.7	0.5	0.4	0.4
SD	0.18	0.22	0.18	0.34	0.19	0.45	0.13
N	8	8	8	8	8	4	4

GROUP: 4-F:1.0 mg base/kg/day

8696	0.2	0.0	1.1	0.9	0.9	--	--
8719	0.3	0.2	1.6	0.5	0.7	--	--
8711	0.1	0.3	2.1	0.6	0.9	--	--
8716	0.1	0.1	2.4	1.0	1.2	--	--
8725	0.3	0.3	0.8	2.1	1.9	0.2	1.0
8707	0.1	0.5	1.1	1.3	2.0	0.6	0.1
8689	0.3	0.1	2.3	0.8	1.8	0.8	0.3
8722	0.3	0.5	1.1	1.4	0.8	0.5	0.3
MEAN	0.2	0.3	1.6	1.1	1.3	0.5	0.4
SD	0.10	0.19	0.63	0.52	0.54	0.25	0.39
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Nucleated Red Cells

STUDY ID: UIC-18

SEX: FEMALE

STUDY NO: 193

ABBR: NRBC

UNITS: COUNT

Animal ID	WEEK 4	WEEK -3	WEEK -1	WEEK 8	WEEK 13	WEEK 18	WEEK 26
GROUP: 1-F:0 mg base/kg/day							
8721	0	0	0	0	0	--	--
8712	0	0	0	0	0	--	--
8710	0	0	0	0	0	--	--
8723	0	0	0	0	0	--	--
8705	0	0	0	0	0	0	0
8700	0	0	0	0	0	0	0
8699	0	0	0	0	0	0	0
8690	0	0	0	0	0	0	0
MEAN	0	0	0	0	0	0	0
SD	0.0	0.0	0.0	0.0	0.0	0.0	0.0
N	8	8	8	8	8	4	4
GROUP: 2-F:0.1 mg base/kg/day							
8717	0	0	0	0	1	--	--
8703	0	0	0	0	0	--	--
8713	0	0	0	0	0	--	--
8693	0	0	0	0	0	--	--
8695	0	0	0	0	0	0	0
8709	0	0	0	0	0	0	0
8715	0	0	0	0	0	0	0
8697	0	0	0	0	0	0	0
MEAN	0	0	0	0	0	0	0
SD	0.0	0.0	0.0	0.0	0.4	0.0	0.0
N	8	8	8	8	8	4	4

WBC corrected for NRBC = or > 10

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Nucleated Red Cells

STUDY ID: UIC-18

SEX: FEMALE

STUDY NO: 193

ABBR: NRBC

UNITS: COUNT

Animal ID	WEEK 4	WEEK -3	WEEK -1	WEEK 8	WEEK 13	WEEK 18	WEEK 26
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GROUP: 3-F:0.3 mg base/kg/day

8692	0	0	0	0	0	--	--
8718	0	0	0	0	0	--	--
8706	0	0	0	0	0	--	--
8714	0	0	0	0	0	--	--
8701	0	0	0	0	0	0	1
8702	0	0	0	0	0	0	0
8720	0	0	0	0	0	0	0
8704	0	0	0	0	0	0	0

MEAN	0	0	0	0	0	0	0
SD	0.0	0.0	0.0	0.0	0.0	0.0	0.5
N	8	8	8	8	8	4	4

GROUP: 4-F:1.0 mg base/kg/day

8696	0	0	0	0	0	--	--
8719	1	0	0	0	0	--	--
8711	29	0	0	0	2	--	--
8716	6	0	0	0	0	--	--
8725	6	0	0	0	0	0	0
8707	0	0	0	0	0	0	0
8689	10	0	0	0	2	0	0
8722	3	0	0	0	0	0	0

MEAN	7	0	0	0	1	0	0
SD	9.6	0.0	0.0	0.0	0.9	0.0	0.0
N	8	8	8	8	8	4	4

WBC corrected for NRBC = or > 10

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Heinz Bodies

STUDY ID: UIC-18

SEX: FEMALE

STUDY NO: 193

ABBR: HEINZ BOD.

UNITS: % RBCs

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
GROUP: 1-F:0 mg base/kg/day							
8721	0.0	0.0	0.0	0.0	0.0	--	--
8712	0.0	0.0	0.0	0.0	0.2	--	--
8710	0.0	0.0	0.0	0.0	0.1	--	--
8723	0.0	0.0	0.0	0.0	0.0	--	--
8705	0.0	0.0	0.0	0.0	0.0	0.0	0.0
8700	0.0	0.0	0.1	0.1	0.0	0.1	0.0
8699	0.0	0.0	0.0	0.0	0.0	0.1	0.2
8690	0.0	0.0	0.0	0.0	0.0	0.0	0.0
MEAN	0.0	0.0	0.0	0.0	0.0	0.1	0.1
SD	0.00	0.00	0.04	0.04	0.07	0.06	0.10
N	8	8	8	8	8	4	4

GROUP: 2-F:0.1 mg base/kg/day							
8717	0.0	0.0	0.0	0.1	0.0	--	--
8703	0.0	0.0	0.0	0.0	0.0	--	--
8713	0.0	0.0	0.0	0.0	0.0	--	--
8693	0.0	0.0	0.0	0.0	0.0	--	--
8695	0.0	0.0	0.0	0.0	0.0	0.0	0.0
8709	0.0	0.0	0.0	0.1	0.0	0.0	0.1
8715	0.0	0.0	0.0	0.0	0.0	0.0	0.0
8697	0.0	0.0	0.0	0.0	0.0	0.0	0.0
MEAN	0.0	0.0	0.0	0.0	0.0	0.0	0.0
SD	0.00	0.00	0.00	0.05	0.00	0.00	0.05
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Heinz Bodies

STUDY ID: UIC-18
STUDY NO: 193
ABBR: HEINZ BOD.

SEX: FEMALE

UNITS: % RBCs

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
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GROUP: 3-F:0.3 mg base/kg/day

8692	0.0	0.0	0.0	0.0	0.0	--	--
8718	0.0	0.0	0.0	0.0	0.0	--	--
8706	0.0	0.0	0.0	0.0	0.0	--	--
8714	0.0	0.0	0.0	0.0	0.0	--	--
8701	0.0	0.0	0.0	0.0	0.0	0.0	3.1
8702	0.0	0.0	0.0	0.1	0.1	0.0	0.0
8720	0.0	0.0	0.0	0.0	0.0	0.0	0.0
8704	0.0	0.0	0.0	0.0	0.0	0.0	0.0

MEAN	0.0	0.0	0.0	0.0	0.0	0.0	0.8
SD	0.00	0.00	0.00	0.04	0.04	0.00	1.55
N	8	8	8	8	8	4	4

GROUP: 4-F:1.0 mg base/kg/day

8696	0.0	0.0	0.0	0.0	0.0	--	--
8719	0.0	0.0	0.0	0.1	0.0	--	--
8711	0.0	0.0	0.0	0.0	0.0	--	--
8716	0.0	0.0	0.0	0.0	0.0	--	--
8725	0.0	0.0	0.0	0.0	0.2	0.0	0.0
8707	0.0	0.0	0.0	0.0	0.0	0.0	0.0
8689	0.0	0.0	0.0	0.0	0.0	0.0	0.0
8722	0.0	0.0	0.0	0.1	0.1	0.0	0.0

MEAN	0.0	0.0	0.0	0.0	0.0	0.0	0.0
SD	0.00	0.00	0.00	0.05	0.07	0.00	0.00
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: % Methemoglobin

STUDY ID: UIC-18
STUDY NO: 193
ABBR: % METHGB

SEX: FEMALE

UNITS: % HGBs

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
GROUP: 1-F:0 mg base/kg/day							
8721	0.5	0.4	0.4	0.7	0.6	--	--
8712	2.3	1.6	0.5	0.6	0.6	--	--
8710	0.2	0.5	0.4	0.6	0.3	--	--
8723	2.2	1.1	1.3	0.9	0.6	--	--
8705	3.0	1.8	0.8	0.8	0.9	0.7	0.7
8700	0.3	0.4	0.7	0.7	0.5	0.6	0.6
8699	0.3	0.6	0.6	0.7	0.5	0.9	0.7
8690	0.7	0.4	1.1	0.7	0.4	0.5	0.9
MEAN	1.2	0.9	0.7	0.7	0.6	0.7	0.7
SD	1.12	0.58	0.33	0.10	0.18	0.17	0.13
N	8	8	8	8	8	4	4

GROUP: 2-F:0.1 mg base/kg/day							
8717	0.8	0.6	1.5	1.6	2.3	--	--
8703	0.3	0.5	2.3	1.6	5.0	--	--
8713	1.1	2.3	2.2	1.6	1.1	--	--
8693	0.7	0.4	2.6	1.9	1.9	--	--
8695	0.3	0.4	3.0	2.6	3.5	0.6	0.5
8709	0.4	0.5	2.8	2.3	2.5	0.6	0.6
8715	1.7	2.2	3.4	2.1	2.4	0.7	0.7
8697	0.2	0.6	2.5	1.8	1.7	0.8	0.7
MEAN	0.7	0.9	2.5	1.9	2.6	0.7	0.6
SD	0.51	0.81	0.57	0.37	1.21	0.10	0.10
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: % Methemoglobin

STUDY ID: UIC-18

SEX: FEMALE

STUDY NO: 193

ABBR: % METHGB

UNITS: % HGBs

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
GROUP: 3-F:0.3 mg base/kg/day							
8692	0.6	0.6	8.7	7.8	9.0	--	--
8718	1.5	0.8	9.1	7.2	6.5	--	--
8706	0.8	0.7	11.3	9.9	8.8	--	--
8714	0.3	0.6	6.4	6.1	5.4	--	--
8701	0.3	0.6	8.1	5.5	6.7	0.6	0.6
8702	2.3	2.3	5.8	4.2	4.7	0.6	0.8
8720	0.8	0.4	10.0	7.5	8.9	0.6	0.6
8704	1.8	1.9	8.3	6.4	5.6	0.6	0.7
MEAN	1.1	1.0	8.5	6.8	7.0	0.6	0.7
SD	0.73	0.70	1.79	1.71	1.73	0.00	0.10
N	8	8	8	8	8	4	4

GROUP: 4-F:1.0 mg base/kg/day							
8696	0.4	0.8	22.9	26.0	21.5	--	--
8719	1.9	1.0	32.0	27.1	28.4	--	--
8711	1.2	1.4	23.4	17.8	16.4	--	--
8716	1.5	1.6	28.5	22.1	24.7	--	--
8725	1.7	1.0	24.1	17.9	20.3	0.9	0.8
8707	0.0	0.6	19.7	14.7	16.7	0.8	0.8
8689	0.3	0.7	26.3	23.2	22.8	0.7	0.8
8722	0.4	0.5	33.2	21.1	24.2	0.7	0.6
MEAN	0.9	1.0	26.3	21.2	21.9	0.8	0.8
SD	0.73	0.39	4.68	4.27	4.07	0.10	0.10
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Platelets

STUDY ID: UIC-18

SEX: FEMALE

STUDY NO: 193

ABBR: PLT

UNITS: $10^3/\text{mm}^3$

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
GROUP: 1-F:0 mg base/kg/day							
8721	336	274	240	285	199	--	--
8712	273	300	247	284	292	--	--
8710	300	258	242	263	202	--	--
8723	334	300	253	259	270	--	--
8705	238	335	209	169	190	182	188
8700	217	206	216	199	159	236	297
8699	255	259	243	213	261	238	231
8690	257	154	217	198	214	251	201
MEAN	276	261	233	234	223	227	229
SD	43.5	57.5	16.7	44.3	45.8	30.6	48.6
N	8	8	8	8	8	4	4
GROUP: 2-F:0.1 mg base/kg/day							
8717	315	258	193	251	204	--	--
8703	287	276	201	200	213	--	--
8713	279	251	187	207	211	--	--
8693	301	276	90	183	180	--	--
8695	246	204	148	201	198	290	346
8709	330	285	277	256	347	281	339
8715	330	288	212	259	246	300	349
8697	299	243	184	262	187	257	249
MEAN	298	260	187	227	223	282	321
SD	28.1	27.9	53.3	32.5	53.8	18.4	48.0
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Platelets

STUDY ID: UIC-18
STUDY NO: 193
ABBR: PLT

SEX: FEMALE

UNITS: $10^3/\text{mm}^3$

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
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GROUP: 3-F:0.3 mg base/kg/day

8692	359	334	202	212	240	--	--
8718	264	265	86	154	107	--	--
8706	197	207	47	103	93	--	--
8714	246	219	62	119	115	--	--
8701	299	160	127	131	142	232	230
8702	316	304	214	281	253	402	382
8720	189	157	86	125	115	215	203
8704	213	212	90	142	142	256	212
MEAN	260	232	114	158	151	276	257
SD	60.8	64.0	62.4	59.4	61.4	85.5	84.3
N	8	8	8	8	8	4	4

GROUP: 4-F:1.0 mg base/kg/day

8696	303	286	133	115	161	--	--
8719	261	243	129	143	247	--	--
8711	249	275	112	226	335	--	--
8716	293	296	61	77	58	--	--
8725	277	260	111	169	290	266	256
8707	187	158	55	29	79	203	163
8689	352	273	110	227	252	342	277
8722	335	346	134	310	387	344	316
MEAN	282	267	106	162	226	289	253
SD	51.9	53.5	31.0	90.8	117.8	67.7	64.9
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Prothrombin Time

STUDY ID: UIC-18
STUDY NO: 193
ABBR: PT

SEX: FEMALE

UNITS: sec

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
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GROUP: 1-F:0 mg base/kg/day

8721	8.3	8.3	8.1	8.0	8.2	--	--
8712	8.3	8.1	8.4	8.5	8.4	--	--
8710	8.3	8.1	8.3	8.5	8.1	--	--
8723	8.2	8.4	8.3	8.4	8.4	--	--
8705	8.2	8.1	8.2	7.9	7.9	8.1	7.8
8700	8.0	8.1	7.8	8.1	8.1	8.2	7.6
8699	8.5	8.7	8.5	8.8	8.5	8.6	8.5
8690	7.8	7.8	8.2	8.2	8.3	8.1	7.9

MEAN	8.2	8.2	8.2	8.3	8.2	8.3	8.0
SD	0.21	0.27	0.21	0.30	0.20	0.24	0.39
N	8	8	8	8	8	4	4

GROUP: 2-F:0.1 mg base/kg/day

8717	8.3	7.8	8.1	8.4	8.4	--	--
8703	8.1	8.2	8.1	8.4	8.4	--	--
8713	8.3	8.3	8.1	8.3	8.2	--	--
8693	8.4	8.6	8.3	8.7	8.5	--	--
8695	8.0	8.3	8.4	8.5	8.2	8.0	8.2
8709	8.2	7.8	8.1	8.3	7.9	7.9	7.8
8715	8.2	8.5	8.5	8.6	8.3	8.2	8.0
8697	8.4	8.6	8.7	8.4	8.5	8.5	8.2

MEAN	8.2	8.3	8.3	8.5	8.3	8.2	8.1
SD	0.14	0.32	0.23	0.14	0.20	0.26	0.19
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Prothrombin Time

STUDY ID: UIC-18
STUDY NO: 193
ABBR: PT

SEX: FEMALE

UNITS: sec

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
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GROUP: 3-F:0.3 mg base/kg/day

8692	8.0	8.4	8.0	8.3	8.3	--	--
8718	8.2	8.0	8.0	8.4	8.1	--	--
8706	8.0	8.1	8.0	7.9	8.1	--	--
8714	8.5	8.5	8.0	8.3	8.0	--	--
8701	7.9	7.8	8.2	8.2	8.0	8.3	7.8
8702	8.3	8.4	8.3	8.4	8.2	8.3	8.0
8720	8.5	8.6	8.3	8.3	8.3	8.4	8.4
8704	8.3	8.1	8.1	8.0	8.3	8.1	7.8

MEAN	8.2	8.2	8.1	8.2	8.2	8.3	8.0
SD	0.23	0.28	0.14	0.18	0.13	0.13	0.28
N	8	8	8	8	8	4	4

GROUP: 4-F:1.0 mg base/kg/day

8696	8.3	8.5	8.4	8.2	8.4	--	--
8719	8.3	8.4	8.0	8.3	8.1	--	--
8711	8.4	8.4	8.0	8.2	8.3	--	--
8716	8.2	8.2	7.7	7.9	7.8	--	--
8725	8.4	8.2	7.9	8.4	8.2	8.3	7.8
8707	8.3	8.2	8.0	8.4	8.0	8.5	8.0
8689	7.8	7.8	7.8	8.2	7.8	7.7	7.6
8722	8.1	8.2	7.9	7.8	7.9	8.3	7.7

MEAN	8.2	8.2	8.0	8.2	8.1	8.2	7.8
SD	0.20	0.21	0.21	0.22	0.23	0.35	0.17
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Act. Partial Thrombo. Time

STUDY ID: UIC-18

SEX: FEMALE

STUDY NO: 193

ABBR: APTT

UNITS: sec

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
GROUP: 1-F:0 mg base/kg/day							
8721	10.2	10.1	10.0	10.3	10.1	--	--
8712	12.4	10.4	9.8	9.7	9.5	--	--
8710	10.2	9.4	9.6	9.7	8.1	--	--
8723	10.6	10.2	9.9	9.8	9.7	--	--
8705	10.7	9.4	9.9	11.0	10.2	9.2	10.0
8700	9.6	9.3	9.6	9.6	8.9	9.0	9.5
8699	11.2	11.0	10.2	11.1	10.6	10.7	10.5
8690	10.7	10.3	10.0	10.2	9.7	10.7	10.7
MEAN	10.7	10.0	9.9	10.2	9.6	9.9	10.2
SD	0.83	0.60	0.21	0.59	0.79	0.93	0.54
N	8	8	8	8	8	4	4
GROUP: 2-F:0.1 mg base/kg/day							
8717	11.0	11.1	10.9	11.0	9.8	--	--
8703	10.3	10.3	10.1	10.0	9.8	--	--
8713	10.0	9.6	9.2	9.7	9.4	--	--
8693	10.3	9.6	10.2	9.5	9.1	--	--
8695	10.1	9.2	9.2	9.6	10.2	9.2	9.9
8709	10.6	9.4	9.8	9.5	9.3	9.0	9.7
8715	11.2	11.0	10.7	10.2	10.4	10.2	10.4
8697	10.3	9.9	9.7	10.2	10.3	9.6	9.8
MEAN	10.5	10.0	10.0	10.0	9.8	9.5	10.0
SD	0.43	0.72	0.63	0.51	0.49	0.53	0.31
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Act. Partial Thrombo. Time

STUDY ID: UIC-18
STUDY NO: 193
ABBR: APTT

SEX: FEMALE

UNITS: sec

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
GROUP: 3-F:0.3 mg base/kg/day							
8692	9.8	9.4	9.6	9.3	9.2	--	--
8718	11.4	10.1	9.5	10.1	9.6	--	--
8706	9.8	9.5	9.3	9.7	9.0	--	--
8714	10.4	8.6	10.0	9.5	9.3	--	--
8701	10.7	11.0	9.5	10.1	10.5	10.1	10.4
8702	10.6	10.1	10.4	10.4	10.4	10.9	10.5
8720	10.9	10.2	10.0	10.1	10.6	10.5	9.9
8704	10.2	9.4	9.7	9.8	9.3	10.1	9.9
MEAN	10.5	9.8	9.8	9.9	9.7	10.4	10.2
SD	0.55	0.72	0.36	0.37	0.65	0.38	0.32
N	8	8	8	8	8	4	4

GROUP: 4-F:1.0 mg base/kg/day							
8696	9.9	10.3	9.5	9.9	8.7	--	--
8719	10.6	9.9	10.0	9.7	10.1	--	--
8711	9.9	9.8	9.3	9.1	9.3	--	--
8716	10.3	9.4	9.8	9.4	9.0	--	--
8725	11.1	10.6	10.3	9.8	9.4	9.8	10.2
8707	10.5	9.9	10.3	9.6	9.7	9.6	10.1
8689	10.9	9.5	10.0	9.7	9.5	10.1	9.7
8722	10.6	10.3	10.7	9.9	10.0	10.2	10.0
MEAN	10.5	10.0	10.0	9.6	9.5	9.9	10.0
SD	0.43	0.41	0.45	0.27	0.47	0.28	0.22
N	8	8	8	8	8	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Leukocytes

STUDY ID: UIC-18
STUDY NO: 193
ABBR: WBC

SEX: FEMALE

UNITS: $10^3/\text{mm}^3$

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
GROUP: 1-F:0 mg base/kg/day							
8721	7.7	7.3	12.2	8.7	9.5	--	--
8712	12.5	8.9	8.3	8.8	10.3	--	--
8710	5.9	6.8	5.7	7.7	6.0	--	--
8723	6.3	6.6	8.6	8.7	7.8	--	--
8705	11.3	12.2	8.5	10.4	10.4	9.2	8.7
8700	8.1	10.5	8.7	7.4	9.3	8.5	8.9
8699	6.3	8.6	10.6	9.6	8.7	8.5	6.3
8690	6.6	5.9	6.8	9.9	7.2	9.1	6.1
MEAN	8.1	8.4	8.7	8.9	8.7	8.8	7.5
SD	2.49	2.15	2.02	1.04	1.55	0.38	1.51
N	8	8	8	8	8	4	4

GROUP: 2-F:0.1 mg base/kg/day							
8717	4.8	11.0	10.9	6.9	7.7	--	--
8703	6.5	8.3	7.2	7.1	7.0	--	--
8713	5.0	7.3	7.5	10.8	6.8	--	--
8693	5.4	7.9	6.0	7.6	6.1	--	--
8695	7.1	6.0	7.1	6.8	8.3	5.8	7.5
8709	8.1	9.1	9.6	8.4	14.6	7.8	9.6
8715	6.8	7.7	9.4	7.9	9.6	6.9	7.9
8697	6.8	6.9	7.5	10.2	6.6	5.5	6.1
MEAN	6.3	8.0	8.2	8.2	8.3	6.5	7.8
SD	1.14	1.52	1.63	1.52	2.76	1.06	1.44
N	8	8	8	8	8	4	4

WBC corrected for NRBC = or > 10

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Leukocytes

STUDY ID: UIC-18
STUDY NO: 193
ABBR: WBC

SEX: FEMALE

UNITS: $10^3/\text{mm}^3$

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	WEEK 13	WEEK 18	WEEK 26
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GROUP: 3-F:0.3 mg base/kg/day

8692	8.9	9.8	11.4	7.6	7.4	--	--
8718	8.7	11.7	9.4	8.6	8.8	--	--
8706	12.6	8.3	6.6	9.4	7.8	--	--
8714	6.1	7.7	7.3	7.5	7.5	--	--
8701	5.0	7.7	9.6	6.8	7.2	6.3	6.9
8702	7.6	10.1	9.8	8.2	8.7	6.8	7.8
8720	7.1	8.6	8.9	9.5	10.7	7.1	6.9
8704	5.8	7.3	7.4	9.4	8.7	7.2	6.9

MEAN	7.7	8.9	8.8	8.4	8.4	6.9	7.1
SD	2.40	1.51	1.60	1.02	1.15	0.40	0.45
N	8	8	8	8	8	4	4

GROUP: 4-F:1.0 mg base/kg/day

8696	5.3	10.1	8.3	18.2	7.8	--	--
8719	8.7	8.7	14.1	12.2	15.5	--	--
8711	5.8	6.8	8.6	7.1	8.9	--	--
8716	5.3	7.1	12.0	11.1	13.5	--	--
8725	8.4	10.8	10.2	13.4	16.9	9.8	10.4
8707	5.5	8.3	7.9	10.9	16.4	6.4	9.0
8689	7.7	8.4	15.8	13.2	18.3	10.2	6.3
8722	6.9	8.5	12.7	10.2	12.8	6.8	6.6

MEAN	6.7	8.6	11.2	12.0	13.8	8.3	8.1
SD	1.42	1.35	2.92	3.19	3.79	1.98	1.97
N	8	8	8	8	8	4	4

WBC corrected for NRBC = or > 10

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18

STUDY NO: 193

GROUP: 1-F : 0 mg base/kg/day

SEX: FEMALE

Animal ID		WEEK -3		WEEK -1		WEEK 4		WEEK 8	
		REL	ABS	REL	ABS	REL	ABS	REL	ABS
8721	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	61.0	4.7	0.0	0.0	66.0	8.1	63.0	5.5
	I. Neutrophils	0.0	0.0	59.0	4.3	0.0	0.0	0.0	0.0
	Lymphocytes	34.0	2.6	0.0	0.0	29.0	3.5	35.0	3.0
	Monocytes	4.0	0.3	33.0	2.4	4.0	0.5	1.0	0.1
	Eosinophils	1.0	0.1	8.0	0.6	1.0	0.1	1.0	0.1
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		7.7		7.3		12.2		8.7
8712	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	72.0	9.0	58.0	5.2	81.0	6.7	62.0	5.5
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	22.0	2.8	35.0	3.1	15.0	1.2	30.0	2.6
	Monocytes	6.0	0.8	5.0	0.4	3.0	0.2	4.0	0.4
	Eosinophils	0.0	0.0	2.0	0.2	1.0	0.1	4.0	0.4
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		12.5		8.9		8.3		8.8
8710	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	60.0	3.5	64.0	4.4	81.0	4.6	80.0	6.2
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	37.0	2.2	30.0	2.0	15.0	0.9	18.0	1.4
	Monocytes	2.0	0.1	5.0	0.3	1.0	0.1	1.0	0.1
	Eosinophils	1.0	0.1	1.0	0.1	3.0	0.2	1.0	0.1
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		5.9		6.8		5.7		7.7

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18

STUDY NO: 193

GROUP: 1-F : 0 mg base/kg/day

SEX: FEMALE

Animal ID		WEEK -3		WEEK -1		WEEK 4		WEEK 8	
		REL	ABS	REL	ABS	REL	ABS	REL	ABS
8723	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	57.0	3.6	66.0	4.4	65.0	5.6	65.0	5.7
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	34.0	2.1	23.0	1.5	29.0	2.5	27.0	2.3
	Monocytes	5.0	0.3	10.0	0.7	3.0	0.3	4.0	0.3
	Eosinophils	4.0	0.3	1.0	0.1	3.0	0.3	4.0	0.3
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		6.3		6.6		8.6		8.7
8705	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	74.0	8.4	67.0	8.2	58.0	4.9	81.0	8.4
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	15.0	1.7	26.0	3.2	28.0	2.4	15.0	1.6
	Monocytes	8.0	0.9	6.0	0.7	1.0	0.1	1.0	0.1
	Eosinophils	3.0	0.3	1.0	0.1	13.0	1.1	3.0	0.3
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		11.3		12.2		8.5		10.4
8700	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	61.0	4.9	64.0	6.7	77.0	6.7	71.0	5.3
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	27.0	2.2	23.0	2.4	17.0	1.5	25.0	1.9
	Monocytes	10.0	0.8	7.0	0.7	3.0	0.3	4.0	0.3
	Eosinophils	2.0	0.2	6.0	0.6	3.0	0.3	0.0	0.0
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		8.1		10.5		8.7		7.4

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18

STUDY NO: 193

GROUP: 1-F : 0 mg base/kg/day

SEX: FEMALE

Animal ID		WEEK -3		WEEK -1		WEEK 4		WEEK 8	
		REL	ABS	REL	ABS	REL	ABS	REL	ABS
8699	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	50.0	3.2	65.0	5.6	55.0	5.8	58.0	5.6
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	36.0	2.3	26.0	2.2	36.0	3.8	40.0	3.8
	Monocytes	7.0	0.4	4.0	0.3	4.0	0.4	1.0	0.1
	Eosinophils	7.0	0.4	5.0	0.4	5.0	0.5	1.0	0.1
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		6.3		8.6		10.6		9.6
8690	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	60.0	4.0	50.0	3.0	67.0	4.6	81.0	8.0
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	28.0	1.8	39.0	2.3	27.0	1.8	13.0	1.3
	Monocytes	12.0	0.8	10.0	0.6	4.0	0.3	2.0	0.2
	Eosinophils	0.0	0.0	1.0	0.1	2.0	0.1	4.0	0.4
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		6.6		5.9		6.8		9.9

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18		GROUP: 2-F : 0.1 mg base/kg/day						SEX: FEMALE	
STUDY NO: 193									
Animal ID		WEEK -3		WEEK -1		WEEK 4		WEEK 8	
		REL	ABS	REL	ABS	REL	ABS	REL	ABS
8717	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	62.0	3.0	75.0	8.3	76.0	8.3	63.0	4.3
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	29.0	1.4	15.0	1.7	18.0	2.0	29.0	2.0
	Monocytes	5.0	0.2	9.0	1.0	4.0	0.4	3.0	0.2
	Eosinophils	4.0	0.2	1.0	0.1	2.0	0.2	5.0	0.3
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		4.8		11.0		10.9		6.9
8703	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	51.0	3.3	61.0	5.1	67.0	4.8	62.0	4.4
	I. Neutrophils	0.0	0.0	1.0	0.1	0.0	0.0	0.0	0.0
	Lymphocytes	39.0	2.5	24.0	2.0	24.0	1.7	31.0	2.2
	Monocytes	8.0	0.5	7.0	0.6	4.0	0.3	4.0	0.3
	Eosinophils	2.0	0.1	7.0	0.6	5.0	0.4	3.0	0.2
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		6.5		8.3		7.2		7.1
8713	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	50.0	2.5	52.0	3.8	64.0	4.8	64.0	6.9
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	43.0	2.2	43.0	3.1	31.0	2.3	28.0	3.0
	Monocytes	4.0	0.2	5.0	0.4	3.0	0.2	6.0	0.6
	Eosinophils	3.0	0.2	0.0	0.0	2.0	0.2	2.0	0.2
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		5.0		7.3		7.5		10.8

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18

STUDY NO: 193

GROUP: 2-F : 0.1 mg base/kg/day

SEX: FEMALE

Animal ID		WEEK -3		WEEK -1		WEEK 4		WEEK 8	
		REL	ABS	REL	ABS	REL	ABS	REL	ABS
8693	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	58.0	3.1	78.0	6.2	55.0	3.3	70.0	5.3
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	32.0	1.7	16.0	1.3	38.0	2.3	25.0	1.9
	Monocytes	7.0	0.4	5.0	0.4	5.0	0.3	5.0	0.4
	Eosinophils	3.0	0.2	1.0	0.1	2.0	0.1	0.0	0.0
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		5.4		7.9		6.0		7.6
8695	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	68.0	4.8	54.0	3.2	56.0	4.0	62.0	4.2
	I. Neutrophils	0.0	0.0	0.0	0.0	6.0	0.4	0.0	0.0
	Lymphocytes	22.0	1.6	39.0	2.3	26.0	1.8	34.0	2.3
	Monocytes	5.0	0.4	4.0	0.2	6.0	0.4	2.0	0.1
	Eosinophils	5.0	0.4	3.0	0.2	3.0	0.2	2.0	0.1
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	3.0	0.2	0.0	0.0
	WBC		7.1		6.0		7.1		6.8
8709	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	65.0	5.3	62.0	5.6	62.0	6.0	67.0	5.6
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	27.0	2.2	32.0	2.9	21.0	2.0	29.0	2.4
	Monocytes	5.0	0.4	5.0	0.5	4.0	0.4	1.0	0.1
	Eosinophils	3.0	0.2	1.0	0.1	13.0	1.2	3.0	0.3
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		8.1		9.1		9.6		8.4

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18

STUDY NO: 193

GROUP: 2-F : 0.1 mg base/kg/day

SEX: FEMALE

Animal ID		WEEK -3		WEEK -1		WEEK 4		WEEK 8	
		REL	ABS	REL	ABS	REL	ABS	REL	ABS
8715	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	49.0	3.3	53.0	4.1	52.0	4.9	62.0	4.9
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	47.0	3.2	35.0	2.7	42.0	3.9	32.0	2.5
	Monocytes	3.0	0.2	7.0	0.5	2.0	0.2	1.0	0.1
	Eosinophils	1.0	0.1	5.0	0.4	4.0	0.4	5.0	0.4
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		6.8		7.7		9.4		7.9
8697	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	62.0	4.2	53.0	3.7	54.0	4.1	82.0	8.4
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	27.0	1.8	37.0	2.6	41.0	3.1	13.0	1.3
	Monocytes	9.0	0.6	9.0	0.6	4.0	0.3	2.0	0.2
	Eosinophils	2.0	0.1	1.0	0.1	1.0	0.1	3.0	0.3
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		6.8		6.9		7.5		10.2

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18

STUDY NO: 193

GROUP: 3-F : 0.3 mg base/kg/day

SEX: FEMALE

Animal ID		WEEK -3		WEEK -1		WEEK 4		WEEK 8	
		REL	ABS	REL	ABS	REL	ABS	REL	ABS
8692	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	43.0	3.8	55.0	5.4	68.0	7.8	51.0	3.9
	I. Neutrophils	0.0	0.0	0.0	0.0	1.0	0.1	0.0	0.0
	Lymphocytes	48.0	4.3	41.0	4.0	28.0	3.2	42.0	3.2
	Monocytes	8.0	0.7	3.0	0.3	2.0	0.2	5.0	0.4
	Eosinophils	1.0	0.1	1.0	0.1	1.0	0.1	2.0	0.2
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		8.9		9.8		11.4		7.6
8718	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	54.0	4.7	65.0	7.6	62.0	5.8	52.0	4.5
	I. Neutrophils	0.0	0.0	0.0	0.0	1.0	0.1	0.0	0.0
	Lymphocytes	33.0	2.9	27.0	3.2	29.0	2.7	40.0	3.4
	Monocytes	10.0	0.9	4.0	0.5	6.0	0.6	3.0	0.3
	Eosinophils	3.0	0.3	4.0	0.5	2.0	0.2	5.0	0.4
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		8.7		11.7		9.4		8.6
8706	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	67.0	8.4	63.0	5.2	62.0	4.1	65.0	6.1
	I. Neutrophils	0.0	0.0	0.0	0.0	2.0	0.1	0.0	0.0
	Lymphocytes	24.0	3.0	25.0	2.1	28.0	1.8	26.0	2.4
	Monocytes	7.0	0.9	9.0	0.7	6.0	0.4	2.0	0.2
	Eosinophils	2.0	0.3	3.0	0.2	2.0	0.1	7.0	0.7
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		12.6		8.3		6.6		9.4

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18

STUDY NO: 193

GROUP: 3-F : 0.3 mg base/kg/day

SEX: FEMALE

Animal ID		WEEK -3		WEEK -1		WEEK 4		WEEK 8	
		REL	ABS	REL	ABS	REL	ABS	REL	ABS
8714	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	44.0	2.7	49.0	3.8	64.0	4.7	72.0	5.4
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	38.0	2.3	45.0	3.5	33.0	2.4	25.0	1.9
	Monocytes	10.0	0.6	5.0	0.4	3.0	0.2	0.0	0.0
	Eosinophils	8.0	0.5	1.0	0.1	0.0	0.0	3.0	0.2
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		6.1		7.7		7.3		7.5
8701	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	42.0	2.1	53.0	4.1	64.0	6.1	55.0	3.7
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	42.0	2.1	43.0	3.3	29.0	2.8	39.0	2.7
	Monocytes	12.0	0.6	3.0	0.2	4.0	0.4	4.0	0.3
	Eosinophils	4.0	0.2	1.0	0.1	3.0	0.3	2.0	0.1
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		5.0		7.7		9.6		6.8
8702	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	55.0	4.2	56.0	5.7	63.0	6.2	67.0	5.5
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	29.0	2.2	33.0	3.3	32.0	3.1	28.0	2.3
	Monocytes	8.0	0.6	8.0	0.8	1.0	0.1	2.0	0.2
	Eosinophils	8.0	0.6	3.0	0.3	4.0	0.4	3.0	0.2
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		7.6		10.1		9.8		8.2

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18		GROUP: 3-F : 0.3 mg base/kg/day						SEX: FEMALE	
STUDY NO: 193									
Animal ID		WEEK -3		WEEK -1		WEEK 4		WEEK 8	
		REL	ABS	REL	ABS	REL	ABS	REL	ABS
8720	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	72.0	5.1	78.0	6.7	75.0	6.7	79.0	7.5
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	19.0	1.3	16.0	1.4	22.0	2.0	17.0	1.6
	Monocytes	6.0	0.4	5.0	0.4	1.0	0.1	2.0	0.2
	Eosinophils	3.0	0.2	1.0	0.1	2.0	0.2	2.0	0.2
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		7.1		8.6		8.9		9.5
8704	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	52.0	3.0	60.0	4.4	61.0	4.5	69.0	6.5
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	37.0	2.1	38.0	2.8	33.0	2.4	22.0	2.1
	Monocytes	8.0	0.5	1.0	0.1	6.0	0.4	6.0	0.6
	Eosinophils	3.0	0.2	1.0	0.1	0.0	0.0	3.0	0.3
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		5.8		7.3		7.4		9.4

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18

STUDY NO: 193

GROUP: 4-F : 1.0 mg base/kg/day

SEX: FEMALE

Animal ID		WEEK -3		WEEK -1		WEEK 4		WEEK 8	
		REL	ABS	REL	ABS	REL	ABS	REL	ABS
8696	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	67.0	3.6	75.0	7.6	77.0	6.4	81.0	14.7
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	1.0	0.2
	Lymphocytes	22.0	1.2	16.0	1.6	23.0	1.9	13.0	2.4
	Monocytes	8.0	0.4	8.0	0.8	0.0	0.0	5.0	0.9
	Eosinophils	3.0	0.2	1.0	0.1	0.0	0.0	0.0	0.0
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		5.3		10.1		8.3		18.2
8719	Nucleated Red Cells	0		0		1		0	
	M. Neutrophils	46.0	4.0	48.0	4.2	76.0	10.7	77.0	9.4
	I. Neutrophils	0.0	0.0	0.0	0.0	1.0	0.1	0.0	0.0
	Lymphocytes	45.0	3.9	48.0	4.2	20.0	2.8	16.0	2.0
	Monocytes	7.0	0.6	3.0	0.3	2.0	0.3	4.0	0.5
	Eosinophils	2.0	0.2	1.0	0.1	1.0	0.1	3.0	0.4
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		8.7		8.7		14.1		12.2
8711	Nucleated Red Cells	0		0		29		0	
	M. Neutrophils	68.0	3.9	69.0	4.7	67.0	5.8	73.0	5.2
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	22.0	1.3	20.0	1.4	20.0	1.7	24.0	1.7
	Monocytes	6.0	0.3	6.0	0.4	6.0	0.5	1.0	0.1
	Eosinophils	4.0	0.2	5.0	0.3	7.0	0.6	2.0	0.1
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		5.8		6.8		8.6		7.1

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18

STUDY NO: 193

GROUP: 4-F : 1.0 mg base/kg/day

SEX: FEMALE

Animal ID		WEEK -3		WEEK -1		WEEK 4		WEEK 8	
		REL	ABS	REL	ABS	REL	ABS	REL	ABS
8716	Nucleated Red Cells	0		0		6		0	
	M. Neutrophils	61.0	3.2	61.0	4.3	77.0	9.2	70.0	7.8
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	32.0	1.7	36.0	2.6	12.0	1.4	21.0	2.3
	Monocytes	6.0	0.3	0.0	0.0	10.0	1.2	4.0	0.4
	Eosinophils	1.0	0.1	3.0	0.2	1.0	0.1	5.0	0.6
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
8725	WBC		5.3		7.1		12.0		11.1
	Nucleated Red Cells	0		0		6		0	
	M. Neutrophils	54.0	4.5	65.0	7.0	56.0	5.7	70.0	9.4
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	34.0	2.9	24.0	2.6	32.0	3.3	26.0	3.5
	Monocytes	8.0	0.7	7.0	0.8	9.0	0.9	2.0	0.3
	Eosinophils	4.0	0.3	4.0	0.4	3.0	0.3	2.0	0.3
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
8707	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		8.4		10.8		10.2		13.4
	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	60.0	3.3	69.0	5.7	68.0	5.4	81.0	8.8
	I. Neutrophils	0.0	0.0	0.0	0.0	1.0	0.1	0.0	0.0
	Lymphocytes	25.0	1.4	21.0	1.7	24.0	1.9	15.0	1.6
	Monocytes	8.0	0.4	9.0	0.7	7.0	0.6	2.0	0.2
	Eosinophils	7.0	0.4	1.0	0.1	0.0	0.0	2.0	0.2
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
8707	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		5.5		8.3		7.9		10.9

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18

STUDY NO: 193

GROUP: 4-F : 1.0 mg base/kg/day

SEX: FEMALE

Animal ID		WEEK -3		WEEK -1		WEEK 4		WEEK 8	
		REL	ABS	REL	ABS	REL	ABS	REL	ABS
8689	Nucleated Red Cells	0		0		10		0	
	M. Neutrophils	49.0	3.8	60.0	5.0	72.0	11.4	68.0	9.0
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	42.0	3.2	28.0	2.4	23.0	3.6	28.0	3.7
	Monocytes	7.0	0.5	5.0	0.4	3.0	0.5	2.0	0.3
	Eosinophils	2.0	0.2	7.0	0.6	2.0	0.3	2.0	0.3
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		7.7		8.4		15.8		13.2
8722	Nucleated Red Cells	0		0		3		0	
	M. Neutrophils	62.0	4.3	53.0	4.5	76.0	9.7	78.0	8.0
	I. Neutrophils	1.0	0.1	0.0	0.0	2.0	0.3	0.0	0.0
	Lymphocytes	31.0	2.1	35.0	3.0	18.0	2.3	14.0	1.4
	Monocytes	6.0	0.4	11.0	0.9	3.0	0.4	5.0	0.5
	Eosinophils	0.0	0.0	1.0	0.1	1.0	0.1	3.0	0.3
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		6.9		8.5		12.7		10.2

WBC corrected for NRBC = or > 10

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18

STUDY NO: 193

GROUP: 1-F : 0 mg base/kg/day

SEX: FEMALE

Animal ID		WEEK 13		WEEK 18		WEEK 26	
		REL	ABS	REL	ABS	REL	ABS
8721	Nucleated Red Cells	0		0		0	
	M. Neutrophils	62.0	5.9	0	--	0	--
	I. Neutrophils	0.0	0.0	0	--	0	--
	Lymphocytes	30.0	2.9	0	--	0	--
	Monocytes	5.0	0.5	0	--	0	--
	Eosinophils	3.0	0.3	0	--	0	--
	Basophils	0.0	0.0	0	--	0	--
	Atypical Lymphocytes	0.0	0.0	0	--	0	--
	Metamyelocytes	0.0	0.0	0	--	0	--
	WBC		9.5		--		--
8712	Nucleated Red Cells	0		0		0	
	M. Neutrophils	66.0	6.8	0	--	0	--
	I. Neutrophils	0.0	0.0	0	--	0	--
	Lymphocytes	29.0	3.0	0	--	0	--
	Monocytes	2.0	0.2	0	--	0	--
	Eosinophils	3.0	0.3	0	--	0	--
	Basophils	0.0	0.0	0	--	0	--
	Atypical Lymphocytes	0.0	0.0	0	--	0	--
	Metamyelocytes	0.0	0.0	0	--	0	--
	WBC		10.3		--		--
8710	Nucleated Red Cells	0		0		0	
	M. Neutrophils	65.0	3.9	0	--	0	--
	I. Neutrophils	0.0	0.0	0	--	0	--
	Lymphocytes	33.0	2.0	0	--	0	--
	Monocytes	1.0	0.1	0	--	0	--
	Eosinophils	1.0	0.1	0	--	0	--
	Basophils	0.0	0.0	0	--	0	--
	Atypical Lymphocytes	0.0	0.0	0	--	0	--
	Metamyelocytes	0.0	0.0	0	--	0	--
	WBC		6.0		--		--

WBC corrected for NRBC = or > 10

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18

STUDY NO: 193

GROUP: 1-F : 0 mg base/kg/day

SEX: FEMALE

Animal ID		WEEK 13		WEEK 18		WEEK 26	
		REL	ABS	REL	ABS	REL	ABS
8723	Nucleated Red Cells	0		0		0	
	M. Neutrophils	57.0	4.4	0	--	0	--
	I. Neutrophils	0.0	0.0	0	--	0	--
	Lymphocytes	38.0	3.0	0	--	0	--
	Monocytes	1.0	0.1	0	--	0	--
	Eosinophils	4.0	0.3	0	--	0	--
	Basophils	0.0	0.0	0	--	0	--
	Atypical Lymphocytes	0.0	0.0	0	--	0	--
	Metamyelocytes	0.0	0.0	0	--	0	--
	WBC		7.8		--		--
8705	Nucleated Red Cells	0		0		0	
	M. Neutrophils	71.0	7.4	67.0	6.2	63.0	5.5
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	19.0	2.0	18.0	1.7	30.0	2.6
	Monocytes	4.0	0.4	5.0	0.5	3.0	0.3
	Eosinophils	6.0	0.6	10.0	0.9	4.0	0.3
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		10.4		9.2		8.7
8700	Nucleated Red Cells	0		0		0	
	M. Neutrophils	62.0	5.8	62.0	5.3	63.0	5.6
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	31.0	2.9	32.0	2.7	27.0	2.4
	Monocytes	2.0	0.2	2.0	0.2	2.0	0.2
	Eosinophils	5.0	0.5	4.0	0.3	8.0	0.7
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		9.3		8.5		8.9

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18
STUDY NO: 193

GROUP: 1-F : 0 mg base/kg/day

SEX: FEMALE

Animal ID		WEEK 13		WEEK 18		WEEK 26	
		REL	ABS	REL	ABS	REL	ABS
8699	Nucleated Red Cells	0		0		0	
	M. Neutrophils	67.0	5.8	60.0	5.1	49.0	3.1
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	23.0	2.0	32.0	2.7	40.0	2.5
	Monocytes	4.0	0.3	4.0	0.3	2.0	0.1
	Eosinophils	6.0	0.5	4.0	0.3	9.0	0.6
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		8.7		8.5		6.3
8690	Nucleated Red Cells	0		0		0	
	M. Neutrophils	70.0	5.0	61.0	5.6	66.0	4.0
	I. Neutrophils	1.0	0.1	0.0	0.0	0.0	0.0
	Lymphocytes	25.0	1.8	31.0	2.8	30.0	1.8
	Monocytes	3.0	0.2	1.0	0.1	2.0	0.1
	Eosinophils	1.0	0.1	7.0	0.6	2.0	0.1
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		7.2		9.1		6.1

WBC corrected for NRBC = or > 10

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18

STUDY NO: 193

GROUP: 2-F : 0.1 mg base/kg/day

SEX: FEMALE

Animal ID		WEEK 13		WEEK 18		WEEK 26	
		REL	ABS	REL	ABS	REL	ABS
8717	Nucleated Red Cells	1		0		0	
	M. Neutrophils	67.0	5.2	0	--	0	--
	I. Neutrophils	0.0	0.0	0	--	0	--
	Lymphocytes	29.0	2.2	0	--	0	--
	Monocytes	3.0	0.2	0	--	0	--
	Eosinophils	1.0	0.1	0	--	0	--
	Basophils	0.0	0.0	0	--	0	--
	Atypical Lymphocytes	0.0	0.0	0	--	0	--
	Metamyelocytes	0.0	0.0	0	--	0	--
	WBC		7.7		--		--
8703	Nucleated Red Cells	0		0		0	
	M. Neutrophils	70.0	4.9	0	--	0	--
	I. Neutrophils	0.0	0.0	0	--	0	--
	Lymphocytes	26.0	1.8	0	--	0	--
	Monocytes	2.0	0.1	0	--	0	--
	Eosinophils	2.0	0.1	0	--	0	--
	Basophils	0.0	0.0	0	--	0	--
	Atypical Lymphocytes	0.0	0.0	0	--	0	--
	Metamyelocytes	0.0	0.0	0	--	0	--
	WBC		7.0		--		--
8713	Nucleated Red Cells	0		0		0	
	M. Neutrophils	60.0	4.1	0	--	0	--
	I. Neutrophils	0.0	0.0	0	--	0	--
	Lymphocytes	35.0	2.4	0	--	0	--
	Monocytes	4.0	0.3	0	--	0	--
	Eosinophils	1.0	0.1	0	--	0	--
	Basophils	0.0	0.0	0	--	0	--
	Atypical Lymphocytes	0.0	0.0	0	--	0	--
	Metamyelocytes	0.0	0.0	0	--	0	--
	WBC		6.8		--		--

WBC corrected for NRBC = or > 10

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18
STUDY NO: 193

GROUP: 2-F : 0.1 mg base/kg/day

SEX: FEMALE

Animal ID		WEEK 13		WEEK 18		WEEK 26	
		REL	ABS	REL	ABS	REL	ABS
8693	Nucleated Red Cells	0		0		0	
	M. Neutrophils	50.0	3.1	0	--	0	--
	I. Neutrophils	0.0	0.0	0	--	0	--
	Lymphocytes	41.0	2.5	0	--	0	--
	Monocytes	8.0	0.5	0	--	0	--
	Eosinophils	1.0	0.1	0	--	0	--
	Basophils	0.0	0.0	0	--	0	--
	Atypical Lymphocytes	0.0	0.0	0	--	0	--
	Metamyelocytes	0.0	0.0	0	--	0	--
	WBC		6.1		--		--
8695	Nucleated Red Cells	0		0		0	
	M. Neutrophils	54.0	4.5	64.0	3.7	71.0	5.3
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	35.0	2.9	35.0	2.0	26.0	2.0
	Monocytes	6.0	0.5	0.0	0.0	2.0	0.2
	Eosinophils	5.0	0.4	1.0	0.1	1.0	0.1
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		8.3		5.8		7.5
8709	Nucleated Red Cells	0		0		0	
	M. Neutrophils	68.0	9.9	63.0	4.9	58.0	5.6
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	26.0	3.8	34.0	2.7	34.0	3.3
	Monocytes	3.0	0.4	1.0	0.1	1.0	0.1
	Eosinophils	3.0	0.4	2.0	0.2	7.0	0.7
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		14.6		7.8		9.6

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18

STUDY NO: 193

GROUP: 2-F : 0.1 mg base/kg/day

SEX: FEMALE

Animal ID		WEEK 13		WEEK 18		WEEK 26	
		REL	ABS	REL	ABS	REL	ABS
8715	Nucleated Red Cells	0		0		0	
	M. Neutrophils	57.0	5.5	50.0	3.5	55.0	4.3
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	38.0	3.6	40.0	2.8	39.0	3.1
	Monocytes	2.0	0.2	2.0	0.1	1.0	0.1
	Eosinophils	3.0	0.3	8.0	0.6	5.0	0.4
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		9.6		6.9		7.9
8697	Nucleated Red Cells	0		0		0	
	M. Neutrophils	56.0	3.7	62.0	3.4	66.0	4.0
	I. Neutrophils	1.0	0.1	0.0	0.0	0.0	0.0
	Lymphocytes	37.0	2.4	33.0	1.8	29.0	1.8
	Monocytes	4.0	0.3	2.0	0.1	3.0	0.2
	Eosinophils	2.0	0.1	3.0	0.2	2.0	0.1
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		6.6		5.5		6.1

WBC corrected for NRBC = or > 10

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18

STUDY NO: 193

GROUP: 3-F : 0.3 mg base/kg/day

SEX: FEMALE

Animal ID		WEEK 13		WEEK 18		WEEK 26	
		REL	ABS	REL	ABS	REL	ABS
8714	Nucleated Red Cells	0		0		0	
	M. Neutrophils	58.0	4.4	0	--	0	--
	I. Neutrophils	0.0	0.0	0	--	0	--
	Lymphocytes	37.0	2.8	0	--	0	--
	Monocytes	5.0	0.4	0	--	0	--
	Eosinophils	0.0	0.0	0	--	0	--
	Basophils	0.0	0.0	0	--	0	--
	Atypical Lymphocytes	0.0	0.0	0	--	0	--
	Metamyelocytes	0.0	0.0	0	--	0	--
	WBC		7.5		--		--
8701	Nucleated Red Cells	0		0		1	
	M. Neutrophils	54.0	3.9	57.0	3.6	65.0	4.5
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	38.0	2.7	40.0	2.5	34.0	2.3
	Monocytes	2.0	0.1	0.0	0.0	0.0	0.0
	Eosinophils	6.0	0.4	3.0	0.2	1.0	0.1
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		7.2		6.3		6.9
8702	Nucleated Red Cells	0		0		0	
	M. Neutrophils	70.0	6.1	48.0	3.3	69.0	5.4
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	28.0	2.4	41.0	2.8	23.0	1.8
	Monocytes	1.0	0.1	4.0	0.3	3.0	0.2
	Eosinophils	1.0	0.1	7.0	0.5	5.0	0.4
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		8.7		6.8		7.8

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18
STUDY NO: 193

GROUP: 3-F : 0.3 mg base/kg/day

SEX: FEMALE

Animal ID		WEEK 13		WEEK 18		WEEK 26	
		REL	ABS	REL	ABS	REL	ABS
8692	Nucleated Red Cells	0		0		0	
	M. Neutrophils	46.0	3.4	0	--	0	--
	I. Neutrophils	0.0	0.0	0	--	0	--
	Lymphocytes	46.0	3.4	0	--	0	--
	Monocytes	3.0	0.2	0	--	0	--
	Eosinophils	5.0	0.4	0	--	0	--
	Basophils	0.0	0.0	0	--	0	--
	Atypical Lymphocytes	0.0	0.0	0	--	0	--
	Metamyelocytes	0.0	0.0	0	--	0	--
	WBC		7.4		--		--
8718	Nucleated Red Cells	0		0		0	
	M. Neutrophils	54.0	4.8	0	--	0	--
	I. Neutrophils	0.0	0.0	0	--	0	--
	Lymphocytes	36.0	3.2	0	--	0	--
	Monocytes	3.0	0.3	0	--	0	--
	Eosinophils	7.0	0.6	0	--	0	--
	Basophils	0.0	0.0	0	--	0	--
	Atypical Lymphocytes	0.0	0.0	0	--	0	--
	Metamyelocytes	0.0	0.0	0	--	0	--
	WBC		8.8		--		--
8706	Nucleated Red Cells	0		0		0	
	M. Neutrophils	56.0	4.4	0	--	0	--
	I. Neutrophils	0.0	0.0	0	--	0	--
	Lymphocytes	37.0	2.9	0	--	0	--
	Monocytes	6.0	0.5	0	--	0	--
	Eosinophils	1.0	0.1	0	--	0	--
	Basophils	0.0	0.0	0	--	0	--
	Atypical Lymphocytes	0.0	0.0	0	--	0	--
	Metamyelocytes	0.0	0.0	0	--	0	--
	WBC		7.8		--		--

WBC corrected for NRBC = or > 10

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18

STUDY NO: 193

GROUP: 3-F : 0.3 mg base/kg/day

SEX: FEMALE

Animal ID		WEEK 13		WEEK 18		WEEK 26	
		REL	ABS	REL	ABS	REL	ABS
8720	Nucleated Red Cells	0		0		0	
	M. Neutrophils	77.0	8.2	72.0	5.1	68.0	4.7
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	16.0	1.7	25.0	1.8	28.0	1.9
	Monocytes	3.0	0.3	0.0	0.0	0.0	0.0
	Eosinophils	4.0	0.4	3.0	0.2	4.0	0.3
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		10.7		7.1		6.9
8704	Nucleated Red Cells	0		0		0	
	M. Neutrophils	57.0	5.0	53.0	3.8	64.0	4.4
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	32.0	2.8	42.0	3.0	34.0	2.3
	Monocytes	5.0	0.4	3.0	0.2	1.0	0.1
	Eosinophils	6.0	0.5	2.0	0.1	1.0	0.1
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		8.7		7.2		6.9

WBC corrected for NRBC = or > 10

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18
STUDY NO: 193

GROUP: 4-F : 1.0 mg base/kg/day

SEX: FEMALE

Animal ID		WEEK 13		WEEK 18		WEEK 26	
		REL	ABS	REL	ABS	REL	ABS
8696	Nucleated Red Cells	0		0		0	
	M. Neutrophils	74.0	5.8	0	--	0	--
	I. Neutrophils	0.0	0.0	0	--	0	--
	Lymphocytes	20.0	1.6	0	--	0	--
	Monocytes	3.0	0.2	0	--	0	--
	Eosinophils	3.0	0.2	0	--	0	--
	Basophils	0.0	0.0	0	--	0	--
	Atypical Lymphocytes	0.0	0.0	0	--	0	--
	Metamyelocytes	0.0	0.0	0	--	0	--
	WBC		7.8		--		--
8719	Nucleated Red Cells	0		0		0	
	M. Neutrophils	75.0	11.6	0	--	0	--
	I. Neutrophils	0.0	0.0	0	--	0	--
	Lymphocytes	19.0	2.9	0	--	0	--
	Monocytes	3.0	0.5	0	--	0	--
	Eosinophils	3.0	0.5	0	--	0	--
	Basophils	0.0	0.0	0	--	0	--
	Atypical Lymphocytes	0.0	0.0	0	--	0	--
	Metamyelocytes	0.0	0.0	0	--	0	--
	WBC		15.5		--		--
8711	Nucleated Red Cells	2		0		0	
	M. Neutrophils	65.0	5.8	0	--	0	--
	I. Neutrophils	0.0	0.0	0	--	0	--
	Lymphocytes	31.0	2.8	0	--	0	--
	Monocytes	1.0	0.1	0	--	0	--
	Eosinophils	3.0	0.3	0	--	0	--
	Basophils	0.0	0.0	0	--	0	--
	Atypical Lymphocytes	0.0	0.0	0	--	0	--
	Metamyelocytes	0.0	0.0	0	--	0	--
	WBC		8.9		--		--

WBC corrected for NRBC = or > 10

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18
STUDY NO: 193

GROUP: 4-F : 1.0 mg base/kg/day

SEX: FEMALE

Animal ID		WEEK 13		WEEK 18		WEEK 26	
		REL	ABS	REL	ABS	REL	ABS
8716	Nucleated Red Cells	0		0		0	
	M. Neutrophils	72.0	9.7	0	--	0	--
	I. Neutrophils	0.0	0.0	0	--	0	--
	Lymphocytes	14.0	1.9	0	--	0	--
	Monocytes	11.0	1.5	0	--	0	--
	Eosinophils	3.0	0.4	0	--	0	--
	Basophils	0.0	0.0	0	--	0	--
	Atypical Lymphocytes	0.0	0.0	0	--	0	--
	Metamyelocytes	0.0	0.0	0	--	0	--
	WBC		13.5		--		--
8725	Nucleated Red Cells	0		0		0	
	M. Neutrophils	63.0	10.6	72.0	7.1	69.0	7.2
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	32.0	5.4	22.0	2.2	27.0	2.8
	Monocytes	3.0	0.5	3.0	0.3	2.0	0.2
	Eosinophils	2.0	0.3	3.0	0.3	2.0	0.2
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		16.9		9.8		10.4
8707	Nucleated Red Cells	0		0		0	
	M. Neutrophils	83.0	13.6	56.0	3.6	69.0	6.2
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	12.0	2.0	33.0	2.1	28.0	2.5
	Monocytes	3.0	0.5	5.0	0.3	1.0	0.1
	Eosinophils	2.0	0.3	6.0	0.4	2.0	0.2
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		16.4		6.4		9.0

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-18
STUDY NO: 193

GROUP: 4-F : 1.0 mg base/kg/day

SEX: FEMALE

Animal ID		WEEK 13		WEEK 18		WEEK 26	
		REL	ABS	REL	ABS	REL	ABS
8689	Nucleated Red Cells	2		0		0	
	M. Neutrophils	68.0	12.4	74.0	7.5	63.0	4.0
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	25.0	4.6	18.0	1.8	32.0	2.0
	Monocytes	6.0	1.1	4.0	0.4	3.0	0.2
	Eosinophils	1.0	0.2	4.0	0.4	2.0	0.1
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		18.3		10.2		6.3
8722	Nucleated Red Cells	0		0		0	
	M. Neutrophils	75.0	9.6	60.0	4.1	51.0	3.4
	I. Neutrophils	0.0	0.0	0.0	0.0	0.0	0.0
	Lymphocytes	24.0	3.1	37.0	2.5	43.0	2.8
	Monocytes	1.0	0.1	1.0	0.1	4.0	0.3
	Eosinophils	0.0	0.0	2.0	0.1	2.0	0.1
	Basophils	0.0	0.0	0.0	0.0	0.0	0.0
	Atypical Lymphocytes	0.0	0.0	0.0	0.0	0.0	0.0
	Metamyelocytes	0.0	0.0	0.0	0.0	0.0	0.0
	WBC		12.8		6.8		6.6

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: UIC-18
STUDY NO: 193

GROUP: 1-F : 0 mg base/kg/day

SEX: FEMALE

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8
8721	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
8712	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells;Clumped Platelets,Slight	Normal Red Blood Cells
8710	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
8723	Poikilocytes,Slight	Normal Red Blood Cells;Clumped Platelets,Slight	Anisocytosis,Slight	Normal Red Blood Cells
8705	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
8700	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
8699	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells;Clumped Platelets,Slight
8690	Anisocytosis,Slight	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: UIC-18					SEX: FEMALE
STUDY NO: 193		GROUP: 2-F : 0.1 mg base/kg/day			
Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8	
8717	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	
8703	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	
8713	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	
8693	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	Target Cells,Slight	
8695	Normal Red Blood Cells	Anisocytosis,Slight	Normal Red Blood Cells	Normal Red Blood Cells	
8709	Normal Red Blood Cells	Normal Red Blood Cells	Anisocytosis,Slight	Normal Red Blood Cells	
8715	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	
8697	Normal Red Blood Cells;Large Platelets,Slight	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: UIC-18
STUDY NO: 193

GROUP: 3-F : 0.3 mg base/kg/day

SEX: FEMALE

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8
8692	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	Anisocytosis,Slight; Target Cells,Slight
8718	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells;Clumped Platelets,Slight	Anisocytosis,Slight; Large Platelets, Slight
8706	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
8714	Normal Red Blood Cells	Normal Red Blood Cells;Large Platelets,Slight	Anisocytosis,Slight	Normal Red Blood Cells
8701	Normal Red Blood Cells	Normal Red Blood Cells;Clumped Platelets,Slight	Normal Red Blood Cells	Normal Red Blood Cells
8702	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
8720	Normal Red Blood Cells;Clumped Platelets,Slight	Normal Red Blood Cells;Clumped Platelets,Slight	Normal Red Blood Cells	Normal Red Blood Cells
8704	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: UIC-18
STUDY NO: 193

GROUP: 4-F : 1.0 mg base/kg/day

SEX: FEMALE

Animal ID	WEEK -3	WEEK -1	WEEK 4	WEEK 8
8696	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	Anisocytosis,Slight; Target Cells,Slight
8719	Normal Red Blood Cells	Anisocytosis,Slight	Normal Red Blood Cells	Anisocytosis,Slight
8711	Normal Red Blood Cells	Normal Red Blood Cells	Anisocytosis,Slight; Polychromasia,Slight	Normal Red Blood Cells
8716	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells;Large Platelets,Slight	Normal Red Blood Cells
8725	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells;Clumped Platelets,Slight	Normal Red Blood Cells;Clumped Platelets,Slight
8707	Normal Red Blood Cells;Large Platelets,Slight	Normal Red Blood Cells	Large Platelets, Slight;Anisocytosis, Slight	Normal Red Blood Cells
8689	Anisocytosis,Slight	Normal Red Blood Cells	Anisocytosis,Slight; Polychromasia,Slight	Normal Red Blood Cells
8722	Normal Red Blood Cells	Normal Red Blood Cells	Large Platelets, Slight;Polychromasia Slight	Normal Red Blood Cells

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: UIC-18

SEX: FEMALE

STUDY NO: 193

GROUP: 1-F : 0 mg base/kg/day

Animal ID	WEEK 13	WEEK 18	WEEK 26
8721	Anisocytosis,Slight	--	--
8712	Normal Red Blood Cells	--	--
8710	Normal Red Blood Cells	--	--
8723	Anisocytosis,Slight	--	--
8705	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
8700	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
8699	Normal Red Blood Cells	Normal Red Blood Cells	Poikilocytes,Slight
8690	Anisocytosis,Slight	Normal Red Blood Cells	Normal Red Blood Cells

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: UIC-18
STUDY NO: 193

GROUP: 2-F : 0.1 mg base/kg/day

SEX: FEMALE

Animal ID	WEEK 13	WEEK 18	WEEK 26
8717	Normal Red Blood Cells; Large Platelets, Slight	--	--
8703	Normal Red Blood Cells	--	--
8713	Normal Red Blood Cells	--	--
8693	Normal Red Blood Cells; Clumped Platelets, Moderate	--	--
8695	Normal Red Blood Cells; Large Platelets, Slight	Normal Red Blood Cells	Anisocytosis, Slight
8709	Normal Red Blood Cells	Normal Red Blood Cells; Large Platelets	Normal Red Blood Cells
8715	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
8697	Anisocytosis, Slight; Large Platelets, Slight	Normal Red Blood Cells	Clumped Platelets, Slight

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: UIC-18
STUDY NO: 193

GROUP: 3-F : 0.3 mg base/kg/day

SEX: FEMALE

Animal ID	WEEK 13	WEEK 18	WEEK 26
8692	Normal Red Blood Cells	--	--
8718	Anisocytosis,Slight; Large Platelets, Slight	--	--
8706	Anisocytosis,Slight; Clumped Platelets, Slight	--	--
8714	Normal Red Blood Cells;Clumped Platelets,Slight	--	--
8701	Normal Red Blood Cells	Normal Red Blood Cells;Large Platelets	Anisocytosis,Slight
8702	Normal Red Blood Cells	Anisocytosis,Slight	Normal Red Blood Cells
8720	Normal Red Blood Cells	Normal Red Blood Cells	Poikilocytes,Slight; Anisocytosis,Slight
8704	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: UIC-18
STUDY NO: 193

GROUP: 4-F : 1.0 mg base/kg/day

SEX: FEMALE

Animal ID	WEEK 13	WEEK 18	WEEK 26
8696	Normal Red Blood Cells	--	--
8719	Normal Red Blood Cells	--	--
8711	Anisocytosis,Slight	--	--
8716	Anisocytosis,Slight; Polychromasia,Slight	--	--
8725	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
8707	Normal Red Blood Cells;Clumped Platelets,Slight	Normal Red Blood Cells	Normal Red Blood Cells
8689	Anisocytosis,Slight; Polychromasia,Slight	Normal Red Blood Cells	Anisocytosis,Slight
8722	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells

(--) - Data Unavailable

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APPENDIX H
Individual Urinalysis Data

URINALYSIS INFORMATION

DRAFT

A. Abbreviations

APP = Appearance
 SG = Specific Gravity
 PRO = Protein
 GLU = Glucose
 KET = Ketones
 BILI = Bilirubin
 BL = Blood
 URO = Urobilinogen
 LEU = Leukocytes
 NIT = Nitrite
 EPI = Epithelial
 SQ = Squamous
 TRANS = Transitional
 NA = Not Applicable
 TP = Triple Phosphate
 QNS = Quantity Not Sufficient
 Y = Yellow

DY = Dark Yellow
 PY = Pale Yellow
 LY = Light Yellow
 BR = Brown
 AM = Amber
 > = Greater than
 FAT = Fatty
 WH = White
 BY = Bright Yellow
 CL = Colorless
 E = Erythrocyte
 FG = Fine Granular
 CG = Course Granular
 HY = Hyaline
 GR = Granular
 S = Starch
 RC = Red Cell
 WC = Waxy

B. Qualitative Evaluation

Protein: Negative
 Trace
 1+ (30 mg/dl)
 2+ (100 mg/dl)
 3+ (500 mg/dl)

Bilirubin: Negative
 I+ (slight)
 2+ (moderate)
 3+ (marked)

Glucose: Normal
 Trace (1/20 g/dl)
 1+ (1/10 g/dl)
 2+ (1/4 g/dl)
 3+ (1/2 g/dl)
 4+ (1 g/dl)

Blood: Negative
 5-10 Ery/ul
 50 Ery/ul
 250 Ery/ul

Ketones: Negative
 1+ (slight amount)
 2+ (moderate)
 3+ (large)

Leukocytes: Negative
 Trace
 1+ (moderate)
 2+ (marked)

Nitrite: Negative
 Positive

Urobilinogen: Normal
 1+ (1 mg/dl)
 2+ (4 mg/dl)
 3+ (8 mg/dl)
 4+ (12 mg/dl)

C. Microscopic Examination: Five fields are examined.

Casts: av. #/10x field
 RBC's: av. #/45x field
 WBC's: av. #/45x field

Epithelial Cells - Squamous: av. #/45x field
 - Transitional: av. #/45x field
 - Renal: av. #/45x field

Crystals; Bacteria; Sperm; Mucus - 0 = Negative
 1+ = Occasional
 2+ = Seen in every field
 3+ = Large amounts in every field
 4+ = Full fields

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

Male Urinalysis Data (Week -3)

DOSE LEVEL (mg base/kg/day)	ANIMAL NO.	APP	SG	COLOR	NIT	LEU	pH	PROT	GLU g/dl	KET	URO	BILI	BLOOD Ery/ul
0	8688	HAZY	1.066	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8687	HAZY	1.013	Y	POS	TRACE	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8662	TURBID	1.045	Y	POS	1+	8	TRACE	NOR	NEG	NOR	NEG	2+
	8673	HAZY	1.033	Y	POS	1+	9	TRACE	NOR	NEG	NOR	2+	1+
	8667	HAZY	1.093	AM	POS	2+	9	1+	NOR	NEG	1+	2+	NEG
	8654	CLEAR	1.031	1+	POS	TRACE	9	TRACE	NOR	NEG	NOR	NEG	NEG
	8662	CLOUDY	1.078	DY	NEG	NEG	9	1+	NOR	1+	NOR	2+	1+
	8676	HAZY	1.025	Y	NEG	2+	9	1+	NOR	NEG	NOR	2+	1+
0.1	8685	HAZY	1.025	Y	POS	1+	9	TRACE	NOR	NEG	NOR	2+	1+
	8673	HAZY	1.021	Y	POS	2+	9	1+	NOR	1+	NOR	NEG	1+
	8663	HAZY	1.078	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8662	CLOUDY	1.027	DY	POS	TRACE	8	DY	NOR	NEG	NOR	NEG	1+
	8685	HAZY	1.066	Y	NEG	2+	9	2+	NOR	NEG	1+	1+	1+
	8662	HAZY	1.078	Y	NEG	1+	7	TRACE	NOR	NEG	NOR	NEG	1+
	8655	CLOUDY	1.045	DY	POS	TRACE	8	DY	NOR	1+	1+	2+	1+
0.3	8655	HAZY	1.102	AM	NEG	2+	9	TRACE	NOR	NEG	NOR	NEG	NEG
	8676	CLOUDY	1.013	Y	POS	1+	9	NEG	NOR	NEG	NOR	NEG	1+
	8653	HAZY	1.069	Y	NEG	NEG	9	TRACE	NOR	NEG	NOR	2+	NEG
	8662	HAZY	1.069	Y	POS	NEG	9	TRACE	NOR	NEG	NOR	1+	1+
	8655	HAZY	1.021	Y	POS	2+	9	TRACE	NOR	1+	1+	2+	NEG
	8687	HAZY	1.087	DY	POS	NEG	9	1+	NOR	NEG	NOR	2+	1+
	8684	HAZY	1.069	2+	NEG	1+	6	TRACE	NOR	NEG	NOR	NEG	1+
	8662	HAZY	1.021	Y	POS	1+	8	TRACE	NOR	NEG	NOR	NEG	1+
1.0	8688	HAZY	1.027	Y	POS	TRACE	9	TRACE	NOR	NEG	NOR	2+	NEG
	8661	HAZY	1.136	AM	POS	1+	7	1+	NOR	1+	1+	2+	NEG
	8670	CLOUDY	1.078	DY	POS	2+	6	1+	NOR	NEG	1+	2+	1+
	8655	HAZY	1.021	Y	POS	1+	8	TRACE	NOR	NEG	NOR	1+	2+
	8664	HAZY	1.025	LY	POS	1+	7	LY	NOR	NEG	NOR	NEG	NEG
	8675	HAZY	1.084	Y	POS	2+	6	TRACE	NOR	NEG	NOR	NEG	1+
	8683	CLOUDY	1.008	LY	POS	1+	9	TRACE	NOR	NEG	NOR	NEG	1+
	8658	CLOUDY	1.030	Y	POS	2+	7	TRACE	NOR	NEG	NOR	1+	2+
	8652	CLOUDY	1.084	Y	NEG	TRACE	7	NEG	NOR	NEG	NOR	NEG	NEG

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

Male Urinalysis Data (Week -3)

DOSE LEVEL (mg base/kg/day)	ANIMAL NO.	CASTS	RBC	WBC	EPITHELIAL CELLS SQ TRANS RENAL			CRYSTALS	BACTERIA	SPERM	MUCUS	YEAST CELLS
0	8653	3 HY 1 FG	0	0	0	0	0	1+ TP	1+	0	0	0
	8687	1 HY	0	0	5	0	0	0	1+	0	0	0
	8654	1 HY	10	0	2	0	0	1+ TP	1+	0	0	0
	8673	0	0	10	2	0	0	1+ TP	1+	0	0	0
	8653	2 FG 3 HY	0	0	0	0	0	1+ TP	1+	0	0	0
	8654	0	5	0	2	0	0	0	1+	0	0	0
	8680	1 HY	0	0	3	0	0	2+ TP	1+	0	0	0
	8676	0	5	10	5	0	0	1+ TP	1+	0	0	0
0.1	8685	7 HY 1 FG	0	7	4	0	0	1+ TP	1+	0	0	0
	8677	1 HY	5	10	5	0	0	1+ TP	1+	0	0	0
	8680	1 HY	0	0	2	0	0	1+ TP	1+	0	0	0
	8680	1 HY	0	0	3	0	0	0	1+	0	0	0
	8665	2 FG	0	10	5	0	0	1+ TP	1+	1+	0	0
	8668	1 HY	5	10	5	0	0	1+ TP	1+	0	0	0
	8655	3 HY	0	0	5	0	0	1+ TP	1+	0	0	0
	8661	1 HY	0	10	5	0	0	1+ TP	1+	0	0	0
0.3	8674	5 HY	5	7	5	0	0	1+ TP	1+	0	0	0
	8653	3 HY FG	0	0	0	0	0	1+ TP	1+	1+	0	0
	8690	1 HY	0	0	5	0	0	1+ TP	1+	0	0	0
	8668	2 FG	5	10	5	0	0	1+ TP	1+	0	0	0
	8682	0	0	0	5	0	0	1+ TP	1+	0	0	0
	8680	1 HY	5	10	5	0	0	1+ TP	1+	1+	0	0
	8662	10 HY	0	10	5	0	0	1+ TP	1+	0	0	0
	8668	1 HY	5	0	2	0	0	1+ TP	2+	0	0	0
1.0	8661	10 HY	0	0	5	0	0	1+ TP	1+	0	0	0
	8677	10 HY	5	10	5	0	0	0	1+	0	0	0
	8681	3 HY 1 FG	0	0	0	0	0	1+ TP	1+	0	0	0
	8664	1 HY	0	5	1	0	0	1+ TP	1+	0	0	0
	8675	1 HY	0	10	1	0	0	1+ TP	1+	0	0	0
	8683	0	0	5	1	0	0	0	1+	0	0	0
	8658	3 HY	3	10	1	0	0	1+ TP	1+	0	0	0
	8652	2 HY	0	7	1	0	0	1+ TP	1+	0	0	0

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

Male Urinalysis Data (Week 4)

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	APP	SG	COLOR	NIT	LEU	pH	PROT	GLU g/dl	KET	URO	BILI	BLOOD Ery/ul
0	8656	HAZY	1.060	Y	POS	NEG	6	TRACE	NOR	NEG	NOR	3+	1+
	8667	CLEAR	1.050	Y	POS	TRACE	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8666	TURBID	1.052	Y	POS	2+	6	2+	NOR	NEG	1+	NEG	1+
	8673	CLOUDY	1.084	DR	POS	1+	6	2+	NOR	NEG	NOR	NEG	1+
	8667	HAZY	1.084	Y	POS	2+	6	TRACE	NOR	NEG	NOR	2+	1+
	8654	CLOUDY	1.018	LY	POS	2+	7	TRACE	NOR	NEG	NOR	NEG	2+
	8680	CLOUDY	1.052	LY	POS	NEG	6	1+	NOR	NEG	NOR	2+	NEG
	8674	HAZY	1.025	LY	POS	2+	7	2+	NOR	NEG	NOR	NEG	1+
0.1	8688	HAZY	1.098	Y	POS	2+	6	TRACE	NOR	NEG	NOR	2+	1+
	8677	HAZY	1.030	Y	POS	TRACE	7	TRACE	NOR	NEG	NOR	2+	NEG
	8663	CLEAR	1.052	Y	POS	NEG	6	TRACE	NOR	NEG	1+	2+	NEG
	8686	CLEAR	1.021	LY	POS	TRACE	7	TRACE	NOR	NEG	NOR	3+	NEG
	8665	HAZY	1.052	Y	POS	2+	6	TRACE	NOR	NEG	NOR	2+	1+
	8666	CLOUDY	1.060	DY	POS	2+	7	2+	NOR	NEG	NOR	3+	1+
	8655	HAZY	1.084	Y	POS	NEG	6	TRACE	NOR	NEG	NOR	2+	NEG
	8659	TURBID	1.060	AM	POS	2+	6	1+	NOR	NEG	1+	2+	2+
0.3	8674	HAZY	1.022	Y	POS	TRACE	7	TRACE	NOR	NEG	NOR	2+	NEG
	8659	HAZY	1.060	AM	POS	TRACE	6	TRACE	NOR	NEG	NOR	3+	NEG
	8690	HAZY	1.052	Y	NEG	TRACE	6	TRACE	NOR	NEG	NOR	2+	NEG
	8688	HAZY	1.042	LY	NEG	2+	7	TRACE	NOR	NEG	NOR	3+	NEG
	8682	HAZY	1.018	LY	POS	2+	6	TRACE	NOR	NEG	NOR	2+	2+
	8683	HAZY	1.042	Y	POS	2+	6	1+	NOR	NEG	NOR	3+	1+
	8688	TURBID	1.098	BR	POS	2+	6	1+	NOR	NEG	1+	2+	1+
	8688	HAZY	1.030	Y	POS	TRACE	6	2+	NOR	NEG	NOR	2+	1+
1.0	8661	HAZY	1.060	AM	POS	2+	6	TRACE	NOR	NEG	1+	2+	1+
	8670	HAZY	1.075	Y	POS	TRACE	6	TRACE	NOR	NEG	NOR	3+	NEG
	8661	HAZY	1.062	Y	POS	1+	6	TRACE	NOR	NEG	NOR	2+	NEG
	8664	CLEAR	1.008	LY	POS	1+	9	TRACE	NOR	NEG	NOR	1+	NEG
	8675	CLEAR	1.060	DY	POS	2+	6	TRACE	NOR	NEG	NOR	2+	NEG
	8683	CLEAR	1.027	Y	POS	1+	9	TRACE	NOR	NEG	NOR	NEG	NEG
	8658	HAZY	1.090	AM	POS	2+	9	1+	NOR	NEG	1+	2+	1+
	8652	CLEAR	1.015	Y	POS	2+	7	TRACE	NOR	NEG	NOR	1+	1+

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

Male Urinalysis Data (Week 4)

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	CASTS	RBC	WBC	EPITHELIAL CELLS SQ TRANS RENAL			CRYSTALS	BACTERIA	SPERM	MUCUS	YEAST CELLS
0	8656	1 FG	0	0	1	0	0	0	3+	1+	0	0
	8680	6 HY	5	7	1	0	0	2+ TP	1+	1+	0	0
	8660	4 HY	10	33	0	0	0	1+ TP	2+	0	0	0
	8673	6 HY	10	35	1	0	0	1+ TP	1+	1+	0	0
	8681	6 HY	0	16	1	0	0	1+ TP	1+	0	0	0
	8666	2 HY	0	0	1	0	0	1+ TP	3+	0	0	0
	8680	10 HY	0	0	1	0	0	2+ TP	1+	0	0	0
	8676	4 HY	10	17	0	0	0	0	1+	1+	0	0
0.1	8665	4 HY	0	16	0	0	0	1+ TP	1+	1+	0	0
	8677	15 HY 1 FG	0	5	0	0	0	0	1+	1+	0	0
	8663	2 HY	0	0	7	0	0	1+ TP	1+	2+	0	0
	8660	10 HY	0	0	0	0	0	0	1+	0	0	0
	8665	4 HY	0	20	0	0	0	1+ TP	1+	0	0	0
	8666	6 HY	5	16	1	0	0	1+ TP	1+	0	0	0
	8681	3 HY	0	0	1	0	0	1+ TP	3+	1+	0	0
	8659	1 HY 1 FG	10	19	0	0	0	1+ TP	1+	0	0	0
0.3	8674	3 HY	0	0	0	0	0	1+ TP	1+	0	0	0
	8681	0	0	0	0	0	0	1+ TP	2+	1+	0	0
	8660	10 HY	0	0	0	0	0	1+ TP	3+	1+	0	0
	8660	4 HY	0	0	0	0	0	3+ TP	1+	1+	0	0
	8663	4 HY	10	10	0	0	0	1+ TP	3+	0	0	0
	8684	4 HY	10	20	0	0	0	1+ TP	1+	0	0	0
	8684	6 HY	0	20	1	0	0	2+ TP	1+	0	0	0
	8666	10 HY	5	10	7	0	0	0	1+	1+	0	0
1.0	8661	6 HY	0	30	1	0	0	1+ TP	3+	1+	0	0
	8670	4 HY	0	0	0	0	0	1+ TP	1+	1+	0	0
	8681	6 HY	0	10	1	0	0	1+ TP	1+	0	0	0
	8664	5 HY	0	5	0	0	0	0	1+	0	0	0
	8675	5 HY 2 FG	0	20	2	0	0	1+ TP	1+	0	0	0
	8683	2 HY	0	15	0	0	0	2+ TP	1+	0	0	0
	8658	7 HY	12	25	8	0	0	1+ TP	1+	0	0	0
	8652	0	4	12	1	0	0	0	1+	0	0	0

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

Male Urinalysis Data (Week 8)

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	APP	SG	COLOR	NIT	LEU	pH	PROT	GLU g/dl	KET	URO	BILI	BLOOD Ery/ul
0	8656	HAZY	1.072	DY	POS	NEG	6	TRACE	NOR	NEG	1+	3+	NEG
	8687	HAZY	1.030	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8669	HAZY	1.090	Y	NEG	NEG	7	TRACE	NOR	NEG	NOR	NEG	NEG
	8673	HAZY	1.090	Y	NEG	2+	6	TRACE	NOR	NEG	NOR	NEG	1+
	8667	HAZY	1.090	DY	NEG	TRACE	7	TRACE	NOR	NEG	NOR	NEG	1+
	8669	HAZY	1.090	Y	POS	2+	6	TRACE	NOR	NEG	NOR	NEG	1+
	8680	HAZY	1.090	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	1+
	8676	HAZY	1.018	LY	NEG	1+	7	TRACE	NOR	NEG	NOR	3+	NEG
0.1	8685	HAZY	1.090	Y	NEG	NEG	6	NEG	NOR	NEG	NOR	NEG	NEG
	8677	CLOUDY	1.140	AM	NEG	2+	7	3+	NOR	1+	1+	2+	NEG
	8663	CLOUDY	1.090	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	1+
	8686	CLEAR	1.030	LY	POS	LY	7	TRACE	NOR	NEG	1+	3+	NEG
	8665	HAZY	1.090	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8666	CLOUDY	1.048	Y	NEG	1+	6	TRACE	NOR	NEG	NOR	NEG	1+
	8655	CLOUDY	1.090	DY	NEG	3+	7	TRACE	NOR	NEG	NOR	NEG	1+
	8659	CLOUDY	1.105	Y	NEG	1+	6	TRACE	NOR	NEG	NOR	NEG	1+
0.3	8676	CLOUDY	1.024	Y	NEG	NEG	7	TRACE	NOR	NEG	NOR	3+	NEG
	8653	CLEAR	1.054	LY	POS	NEG	6	TRACE	NOR	NEG	1+	3+	NEG
	8660	CLOUDY	1.087	Y	POS	1+	6	1+	NOR	NEG	NOR	NEG	2+
	8668	TURBID	1.087	DY	POS	2+	8	1+	NOR	1+	1+	2+	NEG
	8682	HAZY	1.090	DY	POS	TRACE	6	TRACE	NOR	1+	1+	1+	NEG
	8684	TURBID	1.069	AM	NEG	1+	6	1+	NOR	NEG	1+	3+	1+
	8662	CLOUDY	1.093	AM	NEG	1+	7	TRACE	NOR	NEG	NOR	NEG	2+
	8688	HAZY	1.090	Y	POS	TRACE	5	TRACE	NOR	NEG	1+	1+	1+
1.0	8661	HAZY	1.105	DY	POS	TRACE	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8670	HAZY	1.105	DY	POS	2+	6	1+	NOR	1+	1+	2+	1+
	8681	CLEAR	1.015	LY	POS	2+	6	TRACE	NOR	NEG	NOR	1+	1+
	8664	TURBID	1.087	AM	POS	2+	6	1+	NOR	1+	2+	1+	2+
	8675	CLOUDY	1.063	Y	POS	2+	6	TRACE	NOR	NEG	1+	1+	1+
	8683	HAZY	1.070	LY	NEG	2+	9	TRACE	NOR	NEG	NOR	NEG	NEG
	8658	HAZY	1.044	Y	POS	2+	6	TRACE	NOR	NEG	NOR	NEG	2+
	8652	HAZY	1.064	Y	NEG	1+	8	TRACE	NOR	NEG	NOR	NEG	NEG

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

Male Urinalysis Data (Week 8)

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	CASTS	RBC	WBC	EPITHELIAL CELLS SQ TRANS RENAL			CRYSTALS	BACTERIA	SPERM	MUCUS	YEAST CELLS
0	8656	0	0	0	1	0	0	1+ TP	1+	1+	0	0
	8687	7 HY	0	0	1	0	0	1+ TP	1+	0	0	0
	8684	5 HY	0	0	1	0	0	1+ TP	1+	1+	0	0
	8673	1 HY	0	0	1	0	0	0	1+	1+	0	0
	8687	5 HY	10	0	1	0	0	1+ TP	1+	0	0	0
	8656	5 HY	7	35	2	0	0	0	1+	1+	0	0
	8681	5 HY	10	0	1	0	0	0	1+	1+	0	0
	8676	7 HY	0	0	2	0	0	0	1+	3	0	0
0.1	8685	5 HY 1 FG	0	0	0	0	0	1+ TP	1+	1+	0	0
	8677	7 HY	0	20	2	0	0	1+ TP	1+	1+	0	0
	8663	0	0	0	2	0	0	0	1+	1+	0	0
	8686	0	0	4	1	0	0	1+ TP	1+	1+	0	0
	8665	10 HY	0	0	1	0	0	0	1+	1+	0	0
	8684	5 HY	0	20	2	0	0	0	1+	1+	0	0
	8655	3 HY	10	0	2	0	0	2+ TP	1+	0	0	0
	8681	7 HY	0	20	1	0	0	1+ TP	1+	0	0	0
0.3	8676	2 FG	0	0	2	0	0	0	1+	1+	0	0
	8687	0	0	0	2	0	0	2+ TP	1+	1+	0	0
	8681	7 HY	10	0	2	0	0	1+ TP	1+	1+	0	0
	8668	7 HY	0	14	2	0	0	1+ TP	1+	0	0	0
	8663	5 HY	0	0	2	0	0	2+ TP	1+	1+	0	0
	8684	1 FG	0	22	1	0	0	1+ TP	1+	1+	0	0
	8668	7 HY	10	14	2	0	0	1+ TP	1+	1+	0	0
	8684	1 FG	0	0	2	0	0	0	1+	2+	0	0
1.0	8681	5 HY	0	20	2	0	0	0	1+	2+	0	0
	8677	2 HY	0	25	2	0	0	1+ TP	1+	0	0	0
	8681	0	0	0	2	0	0	0	1+	0	0	0
	8608	0	5	8	0	0	0	1+ TP	1+	0	0	0
	8675	0	5	15	0	0	0	1+ TP	3+	0	0	0
	8683	3 HY	5	15	0	0	0	1+ TP	1+	1+	0	0
	8658	13 HY	15	15	0	0	0	0	1+	1+	0	0
	8652	2 HY	0	19	1	0	0	1+ TP	1+	0	0	0

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

Male Urinalysis Data (Week 13)

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	APP	SG	COLOR	NIT	LEU	pH	PROT	GLU g/dl	KET	URO	BILI	BLOOD Ery/ul
0	8668	TURBID	1.062	DY	NEG	NEG	6	1+	NOR	NEG	NOR	NEG	1+
	8687	HAZY	1.090	Y	NEG	1+	6	TRACE	NOR	NEG	NOR	NEG	1+
	8669	HAZY	1.026	Y	POS	TRACE	8	TRACE	NOR	NEG	NOR	NEG	1+
	8673	CLEAR	1.090	Y	NEG	NEG	8	TRACE	NOR	NEG	NOR	NEG	NEG
	8687	CLOUDY	1.090	DY	POS	1+	8	TRACE	NOR	NEG	NOR	NEG	1+
	8660	HAZY	1.090	Y	POS	NEG	8	NEG	NOR	NEG	NOR	NEG	NEG
	8660	CLOUDY	1.064	DY	POS	NEG	8	1+	NOR	NEG	NOR	NEG	1+
	8676	HAZY	1.023	Y	NEG	NEG	8	TRACE	NOR	NEG	NOR	NEG	1+
0.1	8668	HAZY	1.042	Y	NEG	1+	6	TRACE	NOR	NEG	NOR	NEG	2+
	8673	HAZY	1.102	Y	NEG	NEG	8	TRACE	NOR	NEG	NOR	NEG	NEG
	8663	CLOUDY	1.003	Y	NEG	2+	8	TRACE	NOR	NEG	NOR	NEG	3+
	8686	CLOUDY	1.036	Y	NEG	2+	6	TRACE	NOR	NEG	NOR	NEG	3+
	8665	CLEAR	1.090	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8666	HAZY	1.090	Y	POS	1+	6	TRACE	NOR	NEG	NOR	NEG	1+
	8665	HAZY	1.058	Y	POS	1+	8	1+	NOR	NEG	NOR	NEG	1+
	8659	HAZY	1.090	Y	POS	1+	7	TRACE	NOR	NEG	NOR	NEG	1+
0.3	8674	HAZY	1.124	DY	POS	1+	8	1+	NOR	NEG	NOR	NEG	NEG
	8659	CLEAR	1.090	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8660	HAZY	1.075	DY	NEG	NEG	8	TRACE	NOR	NEG	NOR	NEG	1+
	8668	CLOUDY	1.072	DY	NEG	2+	7	1+	NOR	NEG	NOR	NEG	3+
	8663	HAZY	1.054	Y	POS	2+	8	TRACE	NOR	NEG	NOR	NEG	2+
	8666	CLOUDY	1.090	DY	NEG	1+	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8660	HAZY	1.063	Y	POS	1+	8	TRACE	NOR	NEG	NOR	1+	1+
	8668	HAZY	1.090	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
1.0	8661	TURBID	1.165	BR	NEG	1+	8	TRACE	NOR	NEG	NOR	NEG	3+
	8670	HAZY	1.090	DY	POS	2+	8	TRACE	NOR	NEG	NOR	NEG	3+
	8661	CLOUDY	1.052	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	2+
	8664	CLOUDY	1.032	Y	POS	TRACE	6	TRACE	NOR	NEG	NOR	NEG	2+
	8675	CLOUDY	1.064	DY	NEG	2+	5	TRACE	NOR	NEG	NOR	NEG	3+
	8683	HAZY	1.038	Y	POS	2+	6	TRACE	NOR	NEG	NOR	2+	NEG
	8658	CLOUDY	1.054	Y	POS	2+	6	TRACE	NOR	NEG	NOR	NEG	3+
	8652	HAZY	1.060	Y	POS	2+	6	TRACE	NOR	NEG	1+	2+	1+

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

Male Urinalysis Data (Week 13)

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	CASTS	RBC	WBC	EPITHELIAL CELLS SQ TRANS RENAL			CRYSTALS	BACTERIA	SPERM	MUCUS	YEAST CELLS
0	8656	1 FG	5	0	0	0	0	1+ TP	3+	1+	0	0
	8687	1 FG	5	0	5	0	0	0	1+	1+	0	0
	8669	6 HY	5	0	1	0	0	0	1+	0	0	0
	8673	1 HY 1 FG	6	0	2	0	0	1+ TP	1+	2+	0	0
	8667	7 HY	5	10	1	0	0	1+ TP	1+	1+	0	0
	8654	6 HY	5	0	1	0	0	1+ TP	1+	1+	0	0
	8680	13 HY 1 FG	6	0	2	0	0	0	1+	2+	0	0
	8676	1 HY	5	0	5	0	0	0	1+	0	0	0
0.1	8685	7 HY	10	34	5	0	0	0	1+	1+	0	0
	8677	3 HY	5	0	1	0	0	1+ TP	1+	1+	0	0
	8663	0	130	25	0	0	0	0	3+	0	0	0
	8686	0	250	30	1	0	0	1+ TP	3+	0	0	0
	8665	0	5	0	1	0	0	0	1+	1+	0	0
	8686	5 FG	5	10	1	0	0	0	2+	1+	0	0
	8655	4 FG 2 HY	6	0	2	0	0	1+ TP	1+	2+	0	0
	8659	7 HY	5	10	1	0	0	1+ TP	1+	1+	0	0
0.3	8674	1 HY	0	5	1	0	0	1+ TP	2+	2+	0	0
	8653	3 FG 3 HY	0	0	0	0	0	0	1+	1+	0	0
	8660	4 HY	4	0	1	0	0	1+ TP	1+	1+	0	0
	8668	2 HY	7	20	1	0	0	1+ TP	1+	0	0	0
	8682	3 HY	3	10	0	0	0	1+ TP	1+	0	0	0
	8684	1 FG	0	3	3	0	0	1+ TP	1+	1+	0	0
	8662	3 HY	0	5	2	0	0	1+ TP	2+	0	0	0
	8688	4 HY 1 FG	0	0	2	0	0	0	1+	1+	0	0
1.0	8661	0	10	20	0	0	0	1+ TP	1+	1+	0	0
	8670	0	10	15	0	0	0	1+ TP	2+	1+	0	0
	8681	2 HY	10	0	2	0	0	0	1+	1+	0	0
	8664	3 HY	30	0	0	0	0	0	1+	0	0	0
	8675	1 HY	11	13	1	0	0	1+ TP	1+	0	0	0
	8683	0	0	5	1	0	0	0	1+	0	0	0
	8658	4 HY	15	24	1	0	0	1+ TP	1+	0	0	0
	8652	2 HY 1 FG	10	50	10	0	0	0	1+	2+	0	0

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

Male Urinalysis Data (Week 18)

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	APP	SG	COLOR	NIT	LEU	pH	PROT	GLU g/dl	KET	URO	BILI	BLOOD Ery/wl
0	8680	HAZY	1.042	DY	POS	NEG	7	1+	NOR	NEG	NOR	NEG	NEG
	8667	CLOUDY	1.150	AM	NEG	NEG	5	1+	NOR	NEG	NOR	NEG	NEG
	8654	CLEAR	1.090	Y	NEG	2+	6	TRACE	NOR	NEG	NOR	NEG	1+
	8676	CLOUDY	1.060	DY	NEG	2+	5	2+	NOR	NEG	NOR	NEG	1+
0.1	8665	CLEAR	1.022	Y	POS	2+	5	TRACE	NOR	NEG	NOR	NEG	1+
	8665	CLOUDY	1.090	DY	NEG	1+	6	1+	NOR	NEG	NOR	NEG	2+
	8655	CLOUDY	1.060	DY	NEG	NEG	5	1+	NOR	NEG	NOR	NEG	2+
	8667	HAZY	1.060	DY	NEG	2+	5	2+	NOR	NEG	NOR	NEG	NEG
0.3	8674	HAZY	1.012	DY	POS	1+	5	TRACE	NOR	NEG	NOR	NEG	2+
	8682	CLEAR	1.056	DY	NEG	NEG	6	1+	NOR	NEG	NOR	NEG	1+
	8662	CLEAR	1.090	AM	NEG	1+	6	1+	NOR	NEG	NOR	NEG	NEG
	8665	CLOUDY	1.050	AM	NEG	NEG	5	TRACE	NOR	NEG	NOR	1+	1+
1.0	8674	HAZY	1.060	DY	NEG	NEG	5	TRACE	NOR	NEG	NOR	NEG	NEG
	8683	CLEAR	1.034	Y	NEG	2+	5	TRACE	NOR	NEG	NOR	NEG	1+
	8658	CLOUDY	1.068	AM	NEG	2+	5	1+	NOR	NEG	NOR	NEG	2+
	8652	CLOUDY	1.064	DY	NEG	1+	5	TRACE	NOR	NEG	NOR	NEG	1+

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

Male Urinalysis Data (Week 18)

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	CASTS	RBC	WBC	EPITHELIAL CELLS SQ TRANS RENAL			CRYSTALS	BACTERIA	SPERM	MUCUS	YEAST CELLS
0	8680	25 HY	0	0	2	0	0	1+ TP	1+	1+	0	0
	8667	10 HY	0	0	0	0	0	2+ TP	1+	0	0	0
	8688	4 HY	5	0	0	0	0	0	1+	1+	0	0
	8676	10 HY	0	0	3	0	0	1+ TP	1+	0	0	0
0.1	8665	0	2	0	2	0	0	0	1+	1+	0	0
	8666	20 HY	20	110	2	0	0	0	1+	1+	0	0
	8655	4 HY	0	0	2	0	0	1+ TP	1+	1+	0	0
	8659	5 HY 1 CG	0	10	1	0	0	1+ TP	1+	1+	0	0
0.3	8674	10 HY	12	0	0	0	0	1+ TP	1+	1+	0	0
	8668	2 FG 4 HY	4	0	2	0	0	1+ TP	1+	0	0	0
	8662	10 HY 1 FG	4	0	1	0	0	1+ TP	1+	1+	0	0
	8662	1 HY 1 FG	4	14	2	0	0	0	1+	1+	0	0
1.0	8675	10 HY	0	0	2	2	0	1+ TP	1+	0	0	0
	8683	2 FG	4	35	0	0	0	0	1+	2+	0	0
	8658	2 HY 3 FG	5	30	4	0	0	1+ TP	1+	0	0	0
	8652	1 HY	3	17	2	0	0	0	1+	1+	0	0

THIRTEEN WEEK ORAL TOXICITY STUDY
OF WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

Male Urinalysis Data (Week 26)

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	APP	SG	COLOR	NIT	LEU	pH	PROT	GLU g/dl	KET	URO	BILI	BLOOD Ery/ul
0	8680	HAZY	1.066	Y	POS	NEG	5	TRACE	NOR	NEG	NOR	1+	2+
	8667	HAZY	1.108	DY	POS	NEG	5	TRACE	NOR	NEG	NOR	NEG	NEG
	8666	HAZY	1.036	Y	POS	1+	5	TRACE	NOR	NEG	NOR	NEG	2+
	8675	HAZY	1.026	Y	NEG	2+	5	TRACE	NOR	NEG	NOR	1+	NEG
0.1	8666	HAZY	1.060	Y	NEG	2+	5	TRACE	NOR	NEG	NOR	NEG	NEG
	8666	CLEAR	1.060	Y	POS	TRACE	5	TRACE	NOR	NEG	NOR	NEG	NEG
	8659	CLOUDY	1.060	Y	NEG	TRACE	5	TRACE	NOR	NEG	NOR	NEG	2+
	8659	CLEAR	1.066	DY	NEG	NEG	5	2+	NOR	NEG	NOR	NEG	NEG
0.3	8675	CLOUDY	1.024	Y	POS	2+	5	TRACE	NOR	NEG	NOR	NEG	1+
	8682	CLOUDY	1.060	Y	NEG	1+	6	TRACE	NOR	NEG	NOR	NEG	3+
	8662	HAZY	1.056	Y	NEG	TRACE	5	TRACE	NOR	NEG	NOR	2+	1+
	8666	HAZY	1.060	DY	NEG	NEG	5	1+	NOR	NEG	NOR	2+	2+
1.0	8675	CLOUDY	1.066	Y	POS	2+	5	TRACE	NOR	NEG	NOR	NEG	2+
	8683	HAZY	1.046	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	2+	NEG
	8658	TURBID	1.056	Y	POS	2+	5	TRACE	NOR	NEG	NOR	NEG	2+
	8652	CLOUDY	1.017	LY	POS	1+	7	TRACE	NOR	NEG	NOR	NEG	2+

THIRTEEN WEEK ORAL TOXICITY STUDY
OF WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

Male Urinalysis Data (Week 26)

THIRTEEN WEEK ORAL TOXICITY

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	CASTS	RBC	WBC	EPITHELIAL CELLS SQ TRANS RENAL			CRYSTALS	BACTERIA	SPERM	MUCUS	YEAST CELLS
0	8680	7 HY 2 FG	0	5	0	0	0	1+ TP	1+	1+	0	0
	8667	3 HY	0	5	0	0	0	0	1+	1+	0	0
	8688	6 HY 2 FG	0	5	1	0	0	0	1+	1+	0	0
	8676	0	0	5	4	0	0	0	1+	1+	0	0
0.1	8665	7 HY	0	25	0	0	0	1+ TP	1+	0	0	0
	8666	2 HY	0	0	2	0	0	0	1+	1+	0	0
	8655	5 HY 3 FG	0	0	1	0	0	1+ TP	1+	1+	0	0
	8659	7 HY	0	0	4	0	0	1+ TP	1+	1+	0	0
0.3	8674	2 HY	0	0	4	0	0	0	1+	1+	0	0
	8682	7 HY	23	5	0	0	0	1+ TP	1+	0	0	0
	8662	7 HY	0	16	4	0	0	0	1+	1+	0	0
	8688	2 HY 1 FG	0	5	0	0	0	1+ TP	1+	1+	0	0
1.0	8675	3 FG	25	150	0	0	0	1+ TP	1+	0	0	0
	8683	5 HY	0	0	0	0	0	0	1+	1+	0	0
	8658	2 HY	2	10	0	0	0	0	1+	1+	0	0
	8652	10 HY	0	0	4	0	0	1+ TP	1+	0	0	0

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

Female Urinalysis Data (Week -3)

DOSE LEVEL (mg base/kg/day)	ANIMAL NO.	APP	SG	COLOR	NTT	LEU	pH	PROT	GLU g/dl	KET	URO	BILI	BLOOD Ery/ul
0	8721	HAZY	1.060	Y	POS	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8712	HAZY	1.060	DY	POS	2+	6	TRACE	NOR	NEG	NOR	NEG	1+
	8711	HAZY	1.071	Y	POS	1+	6	TRACE	NOR	NEG	NOR	NEG	1+
	8723	HAZY	1.060	DY	NEG	1+	6	TRACE	NOR	NEG	1+	NEG	NEG
	8705	HAZY	1.075	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	3+
	8706	HAZY	1.050	Y	POS	NEG	7	NEG	NOR	NEG	NOR	NEG	NEG
	8695	CLOUDY	1.061	AM	NEG	TRACE	6	1+	NOR	1+	1+	1+	1+
	8692	HAZY	1.015	DY	POS	NEG	7	TRACE	NOR	NEG	NOR	NEG	1+
0.1	8712	HAZY	1.060	AM	POS	1+	6	1+	NOR	1+	NOR	NEG	NEG
	8706	HAZY	1.061	DY	POS	2+	7	1+	NOR	NEG	NOR	NEG	1+
	8711	HAZY	1.050	Y	POS	NEG	6	TRACE	NOR	NEG	1+	NEG	NEG
	8695	HAZY	1.060	DY	POS	1+	7	1+	NOR	NEG	1+	NEG	1+
	8695	HAZY	1.050	Y	POS	2+	7	1+	NOR	NEG	NOR	NEG	1+
	8706	HAZY	1.025	Y	POS	NEG	7	TRACE	NOR	NEG	NOR	NEG	1+
	8711	HAZY	1.061	DY	NEG	TRACE	6	1+	NOR	NEG	1+	NEG	1+
	8695	HAZY	1.060	Y	POS	TRACE	7	TRACE	NOR	NEG	1+	NEG	1+
0.3	8692	HAZY	1.051	Y	POS	TRACE	7	TRACE	NOR	NEG	NOR	NEG	NEG
	8711	HAZY	1.061	DY	NEG	NEG	6	TRACE	NOR	NEG	1+	NEG	NEG
	8706	HAZY	1.051	Y	NEG	NEG	6	1+	NOR	NEG	NOR	NEG	3+
	8716	HAZY	1.046	Y	NEG	NEG	7	TRACE	NOR	NEG	NOR	NEG	1+
	8701	HAZY	1.046	DY	NEG	1+	6	TRACE	NOR	NEG	NOR	NEG	1+
	8702	HAZY	1.036	Y	POS	1+	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8702	HAZY	1.075	DY	NEG	NEG	6	1+	NOR	NEG	1+	NEG	1+
	8704	HAZY	1.075	DY	NEG	TRACE	6	1+	NOR	NEG	NOR	NEG	1+
1.0	8695	CLOUDY	1.060	DY	NEG	2+	6	2+	NOR	NEG	1+	2+	3+
	8711	HAZY	1.050	Y	POS	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8711	HAZY	1.030	Y	NEG	TRACE	7	1+	NOR	NEG	NOR	NEG	1+
	8716	HAZY	1.044	Y	POS	TRACE	7	TRACE	NOR	NEG	NOR	NEG	NEG
	8725	HAZY	1.062	DY	NEG	TRACE	7	TRACE	NOR	1+	1+	1+	NEG
	8702	HAZY	1.052	DY	POS	NEG	7	TRACE	NOR	NEG	NOR	NEG	NEG
	8689	CLEAR	1.058	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8722	HAZY	1.044	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	1+

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

Female Urinalysis Data (Week -3)

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	CASTS	RBC	WBC	EPITHELIAL CELLS SQ TRANS RENAL			CRYSTALS	BACTERIA	SPERM	MUCUS	YEAST CELLS
0	8720	0	0	0	0	0	0	1+ TP	1+	0	0	0
	8712	1 FG 1 HY	5	30	1	0	0	1+ TP	1+	0	0	0
	8710	1 FG	12	10	3	0	0	0	1+	0	0	0
	8706	2 HY	0	0	1	0	0	1+ TP	1+	0	0	0
	8705	0	12	0	1	0	0	1+ TP	1+	0	0	0
	8700	2 HY	0	0	3	0	0	1+ TP	1+	0	0	1+
	8699	0	0	0	3	0	0	3+ TP	1+	0	0	0
	8695	2 HY	0	0	3	0	0	0	1+	0	0	0
0.1	8717	10 HY 2 FG	5	10	1	0	0	1+ TP	1+	0	0	0
	8709	5 HY	5	15	0	0	0	0	1+	0	0	0
	8713	0	0	0	0	0	0	0	1+	0	0	0
	8699	2 HY	3	0	3	0	0	1+ TP	1+	0	0	0
	8695	2 HY	3	10	3	0	0	1+ TP	1+	0	0	0
	8709	8 FG	0	0	1	0	0	0	1+	0	0	0
	8718	1 FG	10	10	3	0	0	1+ TP	1+	0	0	0
	8697	1 FG	0	0	1	0	0	1+ TP	1+	0	0	0
0.3	8697	2 HY	0	0	3	0	0	1+ TP	1+	0	0	0
	8718	0	3	0	1	0	0	2+ TP	1+	0	0	0
	8706	0	25	0	20	0	0	0	2+	0	0	0
	8718	3 HY	0	0	0	0	0	0	1+	0	0	0
	8701	2 HY	7	10	3	0	0	1+ TP	1+	0	0	0
	8702	10 HY	0	13	1	0	0	1+ TP	2+	0	0	0
	8720	1 FG	0	0	3	0	0	1+ TP	1+	0	0	0
	8704	1 FG 1 HY	5	30	1	0	0	2+ TP	1+	0	0	1+
1.0	8696	1 FG	3	25	0	0	0	1+ TP	1+	0	0	1+
	8718	6 HY	0	0	3	0	0	0	1+	0	0	0
	8718	8 FG	3	0	0	0	0	1+ TP	1+	0	0	0
	8716	12 HY	0	18	3	0	0	1+ TP	1+	0	0	0
	8725	3 HY 1 FG	0	0	2	0	0	2+ TP	1+	0	0	0
	8707	2 HY	0	0	1	2	0	1+ TP	1+	0	0	0
	8689	0	0	9	0	0	0	0	1+	0	0	0
	8722	2 HY 1 FG	0	0	1	0	0	1+ TP	1+	0	0	0

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK-
RECOVERY PERIOD IN DOGS

DRAFT

Female Urinalysis Data (Week 4)

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	APP	SG	COLOR	NIT	LEU	pH	PROT	GLU g/dl	KET	URO	BILI	BLOOD Ery/ul
0	8721	CLOUDY	1.060	Y	POS	NEG	6	1+	NOR	NEG	1+	NEG	NEG
	8710	HAZY	1.033	Y	POS	1+	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8710	HAZY	1.063	AM	POS	1+	6	1+	NOR	NEG	1+	1+	1+
	8705	TURBID	1.063	Y	POS	NEG	7	TRACE	NOR	NEG	1+	NEG	NEG
	8705	CLEAR	1.033	Y	POS	NEG	6	1+	NOR	NEG	NOR	1+	NEG
	8706	HAZY	1.021	LY	POS	NEG	7	TRACE	NOR	NEG	NOR	NEG	NEG
	8690	CLOUDY	1.060	LY	NEG	1+	7	TRACE	NOR	NEG	1+	1+	2+
	8690	CLOUDY	1.022	Y	POS	TRACE	6	1+	NOR	NEG	1+	NEG	2+
0.1	8710	CLEAR	1.033	Y	POS	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8709	TURBID	1.030	Y	POS	TRACE	6	TRACE	NOR	NEG	NOR	2+	1+
	8719	CLEAR	1.063	Y	POS	TRACE	6	1+	NOR	NEG	NOR	NEG	NEG
	8693	HAZY	1.060	LY	POS	TRACE	7	1+	NOR	NEG	1+	NEG	NEG
	8690	HAZY	1.022	LY	POS	TRACE	7	TRACE	NOR	NEG	NOR	NEG	NEG
	8709	HAZY	1.048	LY	POS	TRACE	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8715	HAZY	1.060	Y	POS	NEG	6	TRACE	NOR	NEG	1+	NEG	NEG
	8690	HAZY	1.050	Y	POS	NEG	7	1+	NOR	NEG	1+	NEG	NEG
0.3	8690	CLOUDY	1.053	AM	POS	NEG	7	1+	NOR	NEG	1+	NEG	1+
	8710	HAZY	1.060	Y	POS	NEG	6	1+	NOR	NEG	1+	NEG	NEG
	8706	CLEAR	1.060	Y	POS	TRACE	6	1+	NOR	NEG	1+	1+	NEG
	8714	CLEAR	1.072	Y	POS	NEG	6	TRACE	NOR	NEG	1+	NEG	NEG
	8701	CLEAR	1.066	DY	POS	NEG	6	TRACE	NOR	NEG	1+	NEG	2+
	8702	CLEAR	1.081	AM	POS	NEG	7	1+	NOR	NEG	1+	NEG	NEG
	8720	CLOUDY	1.066	AM	POS	TRACE	7	TRACE	NOR	NEG	1+	NEG	NEG
	8720	HAZY	1.075	Y	POS	NEG	6	TRACE	NOR	NEG	1+	2+	NEG
1.0	8696	HAZY	1.033	AM	POS	NEG	6	TRACE	NOR	NEG	NOR	1+	NEG
	8719	CLOUDY	1.069	AM	NEG	NEG	6	1+	NOR	1+	1+	1+	3+
	8710	CLEAR	1.081	LY	POS	2+	7	TRACE	NOR	NEG	1+	NEG	NEG
	8716	CLEAR	1.063	DY	POS	NEG	6	TRACE	NOR	NEG	NOR	2+	NEG
	8725	HAZY	1.050	Y	POS	TRACE	6	TRACE	NOR	NEG	NOR	NEG	1+
	8702	CLOUDY	1.060	Y	POS	1+	6	TRACE	NOR	NEG	1+	NEG	1+
	8689	CLEAR	1.066	DY	POS	NEG	7	TRACE	NOR	NEG	1+	NEG	2+
	8722	CLOUDY	1.104	AM	POS	TRACE	6	TRACE	NOR	1+	1+	2+	1+

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

Female Urinalysis Data (Week 4)

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	CASTS	RBC	WBC	EPITHELIAL CELLS SQ TRANS RENAL			CRYSTALS	BACTERIA	SPERM	MUCUS	YEAST CELLS
0	8721	10 HY	0	0	4	3	0	2+ TP	1+	0	0	0
	8712	2 HY 1 FG	0	6	1	0	0	0	1+	0	0	0
	8710	8 HY	0	80	1	0	0	0	1+	0	0	0
	8723	1 HY	0	0	0	0	0	1+ TP	1+	0	0	0
	8705	4 HY	0	0	4	0	0	1+ TP	1+	0	0	0
	8700	7 HY 1 FG	0	0	0	0	0	1+ TP	1+	0	0	0
	8699	0	10	5	1	0	0	3+ TP	1+	0	0	0
	8690	3 HY	10	18	1	0	0	1+ TP	1+	0	0	0
0.1	8717	3 HY	0	3	1	0	0	1+ TP	1+	0	0	0
	8703	5 HY	8	5	0	0	0	1+ TP	1+	0	0	0
	8713	2 HY	0	0	0	0	0	1+ TP	1+	0	0	0
	8693	7 HY	0	10	5	0	0	2+ TP	1+	0	0	0
	8695	6 HY	0	4	1	0	0	1+ TP	1+	0	0	0
	8709	6 HY	0	15	3	0	0	1+ TP	1+	0	0	0
	8715	1 HY	0	0	0	0	0	1+ TP	1+	0	0	0
	8697	2 HY	0	0	1	0	0	1+ TP	1+	0	0	0
0.3	8692	2 HY	5	0	3	0	0	1+ TP	1+	0	0	0
	8718	5 HY	0	0	6	0	0	0	1+	0	0	0
	8706	1 FG	0	7	1	0	0	1+ TP	1+	0	0	0
	8714	3 HY	0	0	0	0	0	0	1+	0	0	0
	8701	6 HY	5	0	2	0	0	1+ TP	1+	0	0	0
	8702	0	0	0	2	0	0	1+ TP	1+	0	0	0
	8720	6 HY	0	4	0	1	0	1+ TP	1+	0	0	0
	8704	3 HY 1 FG	0	2	1	0	0	1+ TP	1+	0	0	0
1.0	8696	4 HY	0	0	2	0	0	1+ TP	1+	0	0	0
	8719	10 HY	50	0	3	0	0	0	1+	0	0	0
	8711	3 HY	0	7	0	0	0	1+ TP	1+	0	0	0
	8716	1 HY	0	0	0	0	0	1+ TP	1+	0	0	0
	8725	0	10	5	0	0	0	1+ TP	1+	0	0	0
	8707	1 HY	3	5	1	2	0	0	1+	0	0	0
	8689	4 HY	2	0	2	0	0	1+ TP	1+	0	0	0
	8722	8 HY	6	0	4	0	0	1+ TP	1+	0	0	0

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

Female Urinalysis Data (Week 8)

DOSE LEVEL (mgbase/kg/day)	ANIMAL NO.	APP	SG	COLOR	NIT	LEU	pH	PROT	GLU g/dl	KET	URO	BILI	BLOOD Ery/ul
0	8721	HAZY	1.069	LY	POS	TRACE	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8718	HAZY	1.099	Y	POS	1+	6	TRACE	NOR	1+	1+	2+	1+
	8710	HAZY	1.075	Y	POS	1+	6	1+	NOR	NEG	1+	2+	1+
	8723	HAZY	1.093	DY	POS	1+	6	TRACE	NOR	NEG	1+	2+	NEG
	8706	HAZY	1.093	AM	NEG	NEG	6	1+	NOR	1+	NOR	2+	NEG
	8706	CLOUDY	1.102	DY	POS	NEG	6	TRACE	NOR	1+	1+	1+	2+
	8693	HAZY	1.061	Y	NEG	TRACE	6	TRACE	NOR	NEG	1+	1+	NEG
	8693	CLEAR	1.078	Y	POS	TRACE	6	TRACE	NOR	NEG	1+	NEG	2+
0.1	8718	CLOUDY	1.140	AM	POS	TRACE	6	TRACE	NOR	1+	1+	1+	1+
	8706	CLEAR	1.116	AM	POS	TRACE	6	TRACE	NOR	NEG	1+	2+	NEG
	8718	CLOUDY	1.092	AM	POS	TRACE	7	1+	NOR	NEG	1+	2+	2+
	8693	CLOUDY	1.020	AM	POS	TRACE	6	1+	NOR	1+	1+	1+	2+
	8696	HAZY	1.099	Y	POS	NEG	7	TRACE	NOR	1+	1+	NEG	2+
	8706	TURBID	1.051	Y	POS	TRACE	6	TRACE	NOR	NEG	1+	1+	2+
	8718	HAZY	1.078	AM	POS	TRACE	6	TRACE	NOR	NEG	1+	2+	1+
	8697	TURBID	1.039	Y	NEG	NEG	7	1+	NOR	1+	1+	1+	2+
0.3	8692	HAZY	1.054	Y	POS	NEG	6	1+	NOR	1+	1+	NEG	NEG
	8718	CLEAR	1.064	Y	POS	NEG	6	TRACE	NOR	1+	1+	NEG	NEG
	8706	CLEAR	1.064	DY	POS	NEG	6	TRACE	NOR	1+	1+	1+	NEG
	8716	CLOUDY	1.057	Y	POS	2+	7	1+	NOR	NEG	1+	NEG	2+
	8701	HAZY	1.063	DY	NEG	NEG	6	1+	NOR	1+	1+	2+	NEG
	8707	CLEAR	1.078	Y	POS	TRACE	6	TRACE	NOR	1+	1+	NEG	NEG
	8720	TURBID	1.075	DY	NEG	TRACE	7	1+	NOR	1+	1+	2+	1+
	8704	HAZY	1.084	DY	POS	TRACE	6	TRACE	NOR	1+	1+	NEG	1+
1.0	8696	HAZY	1.093	AM	POS	TRACE	7	1+	NOR	1+	1+	1+	2+
	8710	CLEAR	1.015	LY	POS	1+	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8718	CLOUDY	1.063	Y	POS	2+	6	1+	NOR	1+	1+	NEG	1+
	8716	HAZY	1.075	DY	POS	NEG	6	TRACE	NOR	NEG	1+	2+	NEG
	8725	HAZY	1.051	Y	POS	TRACE	7	TRACE	NOR	1+	1+	2+	NEG
	8707	HAZY	1.067	BY	POS	TRACE	6	2+	NOR	2+	1+	2+	NEG
	8689	HAZY	1.066	Y	NEG	NEG	6	TRACE	NOR	1+	1+	NEG	NEG
	8722	CLEAR	1.054	DY	POS	TRACE	7	TRACE	NOR	1+	1+	1+	NEG

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

Female Urinalysis Data (Week 8)

DOSE LEVEL (mg base/kg/day)	ANIMAL NO.	CASTS	RBC	WBC	EPITHELIAL CELLS SQ TRANS RENAL			CRYSTALS	BACTERIA	SPERM	MUCUS	YEAST CELLS
0	8721	1 HY	0	0	0	0	0	1+ TP	1+	0	0	0
	8712	17 HY	0	3	0	0	0	1+ TP	1+	0	0	0
	8713	0	0	27	0	0	0	1+ TP	1+	0	0	0
	8689	1 HY	0	15	0	0	0	1+ TP	1+	0	0	0
	8705	1 FG 1 HY	0	0	3	0	0	0	1+	0	0	0
	8700	3 HY	0	0	1	0	0	1+ TP	1+	0	0	0
	8695	0	0	0	2	0	0	0	1+	0	0	0
	8696	2 HY	12	3	2	0	0	3+ TP	1+	0	0	0
0.1	8717	1 HY	0	0	0	0	0	1+ TP	1+	0	0	0
	8705	4 HY	0	0	1	0	0	1+ TP	1+	0	0	0
	8713	2 HY	12	3	7	0	0	1+ TP	1+	0	0	0
	8693	3 HY	15	0	0	0	0	1+ TP	1+	0	0	0
	8695	4 HY	0	0	3	0	0	1+ TP	1+	0	0	0
	8706	4 HY	12	12	1	0	0	1+ TP	1+	0	0	0
	8713	1 FG	0	0	0	0	0	1+ TP	1+	0	0	0
	8695	2 HY	12	0	1	0	0	1+ TP	1+	0	0	0
0.3	8692	3 HY	0	0	3	0	0	1+ TP	1+	0	0	0
	8713	0	0	0	0	0	0	0	1+	0	0	0
	8706	4 HY	0	3	3	0	0	0	1+	0	0	0
	8713	2 HY	0	12	2	0	0	1+ TP	1+	0	0	0
	8701	0	0	0	3	0	0	1+ TP	1+	0	0	0
	8702	1 FG	0	12	1	0	0	0	1+	0	0	0
	8720	2 HY	0	3	1	0	0	2+ TP	1+	0	0	0
	8706	2 HY	0	3	1	0	0	0	1+	0	0	0
1.0	8695	4 HY	0	0	3	0	0	1+ TP	1+	0	0	0
	8713	0	0	0	0	0	0	0	1+	0	0	0
	8713	1 HY	0	12	0	0	0	1+ TP	1+	0	0	0
	8716	1 HY	0	0	0	0	0	0	1+	0	0	0
	8725	1 HY	0	0	1	0	0	1+ TP	1+	0	0	0
	8707	2 HY	0	0	0	0	0	1+ TP	1+	0	0	0
	8689	1 HY	0	0	1	0	0	0	1+	0	0	0
	8722	1 HY	0	0	0	0	0	1+ TP	1+	0	0	0

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

Female Urinalysis Data (Week 13)

DOSE LEVEL (mg bssc/kg/day)	ANIMAL NO.	APP	SG	COLOR	NIT	LEU	pH	PROT	GLU g/dl	KET	URO	BILI	BLOOD Ery/ul
0	8721	HAZY	1.044	DY	POS	1+	6	TRACE	NOR	NEG	NOR	NEG	1+
	8717	HAZY	1.090	Y	NEG	NEG	7	NEG	NOR	NEG	NOR	NEG	NEG
	8711	HAZY	1.056	Y	POS	1+	8	TRACE	NOR	NEG	NOR	NEG	1+
	8723	HAZY	1.056	Y	NEG	NEG	7	NEG	NOR	NEG	NOR	NEG	NEG
	8709	HAZY	1.105	DY	NEG	NEG	8	TRACE	NOR	NEG	NOR	NEG	NEG
	8700	HAZY	1.042	Y	POS	TRACE	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8695	HAZY	1.066	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8690	CLEAR	1.052	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
0.1	8717	HAZY	1.105	Y	POS	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8709	HAZY	1.087	DY	NEG	TRACE	8	TRACE	NOR	NEG	NOR	NEG	NEG
	8711	HAZY	1.066	Y	POS	TRACE	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8693	HAZY	1.078	Y	NEG	NEG	6	NEG	NOR	NEG	NOR	NEG	NEG
	8695	HAZY	1.056	Y	NEG	NEG	7	NEG	NOR	NEG	NOR	NEG	NEG
	8709	CLOUDY	1.044	Y	POS	1+	8	TRACE	NOR	NEG	NOR	NEG	1+
	8715	HAZY	1.090	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8697	HAZY	1.018	DY	POS	NEG	7	TRACE	NOR	NEG	NOR	NEG	1+
0.3	8692	HAZY	1.056	Y	NEG	NEG	6	NEG	NOR	NEG	NOR	NEG	NEG
	8718	HAZY	1.090	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8708	HAZY	1.090	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8714	HAZY	1.056	Y	NEG	NEG	5	NEG	NOR	NEG	NOR	NEG	2+
	8701	HAZY	1.099	Y	POS	TRACE	5	TRACE	NOR	NEG	NOR	NEG	1+
	8702	HAZY	1.128	Y	NEG	1+	6	TRACE	NOR	NEG	NOR	NEG	1+
	8706	HAZY	1.052	Y	NEG	NEG	7	TRACE	NOR	NEG	NOR	NEG	NEG
	8704	CLOUDY	1.072	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	1+
1.0	8698	HAZY	1.090	Y	POS	TRACE	8	TRACE	NOR	NEG	NOR	2+	1+
	8715	HAZY	1.130	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8711	HAZY	1.066	Y	POS	NEG	7	TRACE	NOR	NEG	NOR	NEG	NEG
	8714	HAZY	1.072	DY	POS	TRACE	6	TRACE	NOR	NEG	NOR	NEG	1+
	8725	HAZY	1.066	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	1+
	8707	HAZY	1.066	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8689	HAZY	1.040	LY	POS	NEG	5	TRACE	NOR	NEG	NOR	NEG	1+
	8722	HAZY	1.150	AM	NEG	TRACE	6	TRACE	NOR	NEG	NOR	NEG	NEG

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

Female Urinalysis Data (Week 13)

DOSE LEVEL (mg base/kg/day)	ANIMAL NO.	CASTS	RBC	WBC	EPITHELIAL CELLS SQ TRANS RENAL			CRYSTALS	BACTERIA	SPERM	MUCUS	YEAST CELLS
0	8721	2 HY	0	2	1	0	0	0	1+	0	0	0
	8714	5 HY	0	0	1	0	0	1+ TP	1+	0	0	0
	8716	0	0	14	1	0	0	1+ TP	1+	0	0	0
	8723	0	0	0	1	0	0	1+ TP	0	0	0	0
	8705	7 HY	0	0	1	0	0	1+ TP	1+	0	0	0
	8706	2 HY	0	0	0	0	0	0	1+	0	0	0
	8699	5 HY 1 FG	0	0	2	0	0	0	1+	0	0	0
	8692	2 HY	0	0	0	0	0	1+ TP	1+	0	0	0
0.1	8718	0	0	0	1	0	0	1+ TP	1+	0	0	0
	8703	2 HY	0	0	1	0	0	1+ TP	1+	0	0	0
	8714	3 HY	0	0	1	0	0	0	1+	0	0	0
	8693	2 HY	0	0	2	0	0	0	1+	0	0	0
	8692	2 HY	0	0	1	0	0	0	1+	0	0	0
	8706	2 HY	12	0	1	0	0	0	1+	0	0	0
	8714	4 HY	0	0	1	0	0	1+ TP	1+	0	0	0
	8692	0	0	0	2	0	0	0	1+	0	0	0
0.3	8692	2 HY	0	0	1	0	0	0	1+	0	0	0
	8718	2 HY	0	0	1	0	0	1+ TP	1+	0	0	0
	8706	0	0	0	2	0	0	1+ TP	1+	0	0	0
	8714	2 HY	15	0	2	0	0	0	1+	0	0	0
	8701	4 HY	0	0	1	2	0	0	1+	0	0	0
	8702	2 HY	0	13	1	0	0	0	1+	0	0	0
	8706	4 HY	0	0	1	0	0	1+ TP	1+	0	0	0
	8706	4 HY	12	0	1	0	0	1+ TP	1+	0	0	0
1.0	8696	4 HY	0	0	1	0	0	1+ TP	1+	1+	0	0
	8714	2 HY	0	0	1	0	0	1+ TP	1+	0	0	0
	8714	4 HY	0	0	3	0	0	1+ TP	1+	0	0	0
	8716	1 HY	0	0	5	2	0	0	1+	0	0	0
	8725	1 HY	0	0	3	0	0	1+ TP	1+	0	0	0
	8707	1 HY	0	0	3	0	0	0	1+	0	0	0
	8689	1 HY	0	0	1	0	0	0	1+	0	0	0
	8722	4 HY	2	0	2	0	0	1+ TP	1+	0	0	0

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

Female Urinalysis Data (Week 18)

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	APP	SG	COLOR	NIT	LEU	pH	PROT	GLU g/dl	KET	URO	BILI	BLOOD Ery/wl
0	8709	CLOUDY	1.034	Y	POS	NEG	7	NEG	NOR	NEG	NOR	NEG	NEG
	8709	CLOUDY	1.046	BY	POS	NEG	6	NEG	NOR	NEG	NOR	NEG	1+
	8699	CLOUDY	1.060	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8690	CLOUDY	1.058	Y	POS	NEG	6	TRACE	NOR	NEG	NOR	NEG	1+
0.1	8695	CLOUDY	1.052	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	1+
	8709	CLOUDY	1.056	DY	POS	1+	6	TRACE	NOR	NEG	NOR	NEG	2+
	8715	TURBID	1.046	AM	POS	NEG	6	TRACE	NOR	NEG	NOR	NEG	2+
	8697	CLOUDY	1.034	Y	NEG	NEG	7	TRACE	NOR	NEG	NOR	NEG	NEG
0.3	8701	CLOUDY	1.052	Y	POS	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8702	CLOUDY	1.038	LY	POS	TRACE	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8709	CLOUDY	1.081	DY	POS	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8704	CLOUDY	1.063	Y	POS	NEG	6	TRACE	NOR	NEG	NOR	NEG	1+
1.0	8725	CLOUDY	1.028	LY	POS	NEG	6	TRACE	NOR	NEG	NOR	NEG	2+
	8707	CLOUDY	1.052	Y	POS	NEG	5	TRACE	NOR	NEG	NOR	NEG	NEG
	8689	CLOUDY	1.025	PY	POS	TRACE	6	TRACE	NOR	NEG	NOR	NEG	1+
	8722	CLOUDY	1.066	Y	POS	TRACE	7	TRACE	NOR	NEG	NOR	NEG	1+

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

Female Urinalysis Data (Week 18)

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	CASTS	RBC	WBC	EPITHELIAL CELLS SQ TRANS RENAL			CRYSTALS	BACTERIA	SPERM	MUCUS	YEAST CELLS
0	8705	8 HY	0	0	3	0	0	1+ TP	1+	0	0	0
	8706	2 HY	0	0	3	0	0	1+ TP	1+	0	0	0
	8695	3 HY	0	0	0	0	0	1+ TP	1+	0	0	0
	8696	4 HY	14	0	0	0	0	0	1+	0	0	0
0.1	8695	3 HY	0	3	0	0	0	1+ TP	1+	0	0	0
	8706	4 HY	0	3	0	0	0	1+ TP	1+	0	0	0
	8715	5 HY	0	0	3	0	0	1+ TP	1+	0	0	0
	8697	1 FG	0	0	0	0	0	1+ TP	1+	0	0	0
0.3	8701	3 HY	0	0	0	0	0	1+ TP	1+	0	0	0
	8702	3 HY	3	7	0	3	0	0	1+	0	0	0
	8702	8 HY	0	0	3	0	0	1+ TP	1+	0	0	0
	8704	8 HY	0	0	2	0	0	1+ TP	1+	0	0	0
1.0	8725	4 HY	0	3	0	0	0	0	1+	0	0	1+
	8707	3 HY	0	0	1	0	0	1+ TP	1+	0	0	0
	8689	2 HY	0	0	0	0	0	0	2+	0	0	0
	8722	1 FG	0	2	3	0	0	0	1+	0	0	0

^a 100 mg/kg/day (DAYS 0-29) / 50 mg/kg/day (DAYS 38-91)

^b Animal sacrificed on Day 27

THIRTEEN WEEK ORAL TOXICITY STUDY
OF WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

Female Urinalysis Data (Week 26)

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	APP	SG	COLOR	NIT	LEU	pH	PROT	GLU g/dl	KET	URO	BILI	BLOOD Ery/ul
0	8705	CLOUDY	1.081	DY	NEG	NEG	5	TRACE	NOR	NEG	NOR	NEG	1+
	8720	CLEAR	1.060	DY	POS	NEG	5	TRACE	NOR	NEG	NOR	NEG	NEG
	8699	CLOUDY	1.056	Y	NEG	NEG	5	TRACE	NOR	NEG	NOR	NEG	NEG
	8690	CLEAR	1.060	Y	NEG	NEG	5	TRACE	NOR	NEG	NOR	NEG	NEG
0.1	8695	HAZY	1.060	Y	NEG	NEG	5	TRACE	NOR	NEG	NOR	NEG	NEG
	8720	CLEAR	1.060	Y	NEG	NEG	5	TRACE	NOR	NEG	NOR	NEG	NEG
	8715	CLOUDY	1.050	Y	NEG	NEG	5	TRACE	1+	NEG	NOR	NEG	1+
	8697	CLEAR	1.027	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	1+
0.3	8701	CLEAR	1.056	Y	POS	NEG	5	TRACE	NOR	NEG	NOR	NEG	NEG
	8720	CLEAR	1.046	LY	POS	NEG	5	NEG	NOR	NEG	NOR	NEG	NEG
	8720	CLEAR	1.186	AM	POS	NEG	5	1+	NOR	NEG	NOR	NEG	NEG
	8720	HAZY	1.062	Y	NEG	NEG	5	TRACE	NOR	NEG	NOR	NEG	NEG
1.0	8706	TURBID	1.025	Y	NEG	1+	5	1+	NOR	NEG	NOR	NEG	2+
	8707	HAZY	1.165	DY	POS	NEG	5	TRACE	NOR	NEG	NOR	NEG	NEG
	8689	CLOUDY	1.040	Y	POS	TRACE	5	TRACE	NOR	NEG	NOR	NEG	2+
	8722	CLEAR	1.096	Y	POS	NEG	6	TRACE	NOR	NEG	NOR	NEG	1+

THIRTEEN WEEK ORAL TOXICITY STUDY
OF WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

Female Urinalysis Data (Week 26)

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	CASTS	RBC	WBC	EPITHELIAL CELLS SQ TRANS RENAL			CRYSTALS	BACTERIA	SPERM	MUCUS	YEAST CELLS
0	8703	1 FG	0	0	1	7	0	0	1+	0	0	0
	8700	1 HY	0	0	1	0	0	0	1+	0	0	0
	8695	1 HY	0	0	4	0	0	1+ TP	1+	0	0	0
	8695	1 HY	0	0	4	0	0	0	1+	0	0	0
0.1	8695	1 HY	0	0	1	0	0	1+ TP	1+	0	0	0
	8708	1 HY	0	0	0	0	0	0	1+	0	0	0
	8715	1 HY	0	0	4	0	0	2+ TP	1+	0	0	0
	8695	1 HY	0	0	1	7	0	0	1+	0	0	0
0.3	8701	0	0	0	1	0	0	0	1+	0	0	0
	8708	0	0	0	0	0	0	0	1+	0	0	0
	8720	1 HY	0	0	0	0	0	1+ TP	1+	0	0	0
	8708	0	0	0	4	0	0	0	1+	0	0	0
1.0	8725	3 HY 1 FG	5	3	0	0	0	1+ TP	1+	0	0	0
	8707	1 HY	0	0	7	5	0	1+ TP	1+	0	0	0
	8689	1 HY	0	0	0	0	0	0	1+	0	0	0
	8722	2 HY	0	0	3	0	0	1+ TP	1+	0	0	0

DRAFT

APPENDIX I
Cardiology Report

April 15, 1996

D R A F T

TO: Dr. Barry S. Levine
Director
Toxicology Research Laboratory
1940 West Taylor Street
Chicago, Illinois 60612-7353

A handwritten signature in black ink, appearing to be 'M. L. Hamlin', is located to the right of the TO: address.

FROM: Robert L. Hamlin, DVM, PhD
Diplomate ACVIM (Cardiology/Internal Medicine)
1520 Grenoble Road
Columbus, Ohio 43221

RE: Analysis of ECGs from beagle dogs on UIC/TRL Study No. 193
entitled "Thirteen week oral toxicity study of WR242511 with
thirteen week recovery period in dogs."

All ECGs are within limits of normal. All dogs remained in sinus
rhythms. There were no systematic changes either qualitative or
quantitative that appeared to be drug-related.

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

Electrocardiogram Diagnosis of Males

Dose (mg base/kg/day)	Animal Number	Week -3	Week 13	Week 26
0	8654	WNL	WNL	WNL
	8656	WNL	WNL	-
	8654	WNL	WNL	WNL
	8654	WNL	WNL	-
	8673	WNL	WNL	-
	8676	PWNL (RAD)	WNL	WNL
	8654	WNL	WNL	WNL
	8687	WNL	WNL	-
0.1	8655	WNL	WNL	WNL
	8655	WNL	WNL	WNL
	8663	WNL	WNL	-
	8665	WNL	WNL	WNL
	8666	WNL	WNL	WNL
	8677	WNL	WNL	-
	8655	WNL	WNL	-
	8686	WNL	WNL	-
0.3	8654	WNL	WNL	-
	8660	WNL	WNL	-
	8661	WNL	WNL	WNL
	8661	WNL	WNL	-
	8674	WNL	WNL	WNL
	8658	WNL	WNL	WNL
	8654	WNL	WNL	-
	8661	WNL	WNL (LAD)	WNL (IRBBB)
1.0	8652	WNL	WNL	WNL
	8658	PWNL (IVCD)	WNL	WNL
	8661	WNL	WNL	-
	8664	PWNL (BP)	WNL	-
	8676	WNL	WNL	-
	8675	WNL	WNL	WNL
	8681	WNL	WNL	-
	8683	WNL	WNL	WNL

- = Animal previously sacrificed
WNL = Within normal limits
PWNL = Probably within normal limits
RAD = Right axis deviation
LAD = Left axis deviation
PP = Peaked P

LT = Large Ta
LTW = Large Ta Waves
BP = Broad P
IVCD = Interventricular conduction disturbance
IRBBB = Incomplete right bundle branch block

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

D R A F T

Electrocardiogram Diagnosis of Females

Dose (mg base/kg/day)	Animal Number	Week -3	Week 13	Week 26
0	8690	WNL	WNL	WNL
	8690	WNL	WNL	WNL
	8701	WNL	WNL (LTW)	WNL
	8705	WNL	WNL	WNL
	8701	WNL	WNL	-
	8712	WNL	WNL	-
	8701	WNL	WNL	-
	8723	WNL	WNL	-
0.1	8693	WNL	WNL	-
	8695	WNL	WNL	WNL
	8697	WNL (RAD)	WNL	WNL
	8703	WNL	WNL	-
	8701	WNL	WNL	WNL
	8713	WNL	WNL	-
	8715	WNL	WNL	WNL
	8717	WNL (RAD)	WNL	-
0.3	8692	WNL	WNL	-
	8701	WNL	WNL	WNL
	8702	WNL	WNL	WNL
	8704	WNL	WNL	WNL
	8705	PWNL (RAD)	WNL (IRBBB)	-
	8714	WNL	WNL	-
	8718	WNL	WNL	-
	8720	WNL	WNL	WNL
1.0	8689	PWNL (PP, LT)	WNL	WNL
	8696	WNL	WNL	-
	8707	WNL (RAD)	WNL (IRBBB)	WNL (IRBBB)
	8711	WNL	WNL	-
	8716	PWNL (RAD)	WNL	-
	8719	WNL	WNL	-
	8722	WNL	WNL	WNL
	8725	WNL	WNL	WNL

- = Animal previously sacrificed
WNL = Within normal limits
PWNL = Probably within normal limits
RAD = Right axis deviation
LAD = Left axis deviation
PP = Peaked P

LT = Large T_a
LTW = Large T_a Waves
BP = Broad P
IVCD = Interventricular conduction disturbance
IRBBB = Incomplete right bundle branch block

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

SUMMARY REPORT
TEST: Heart Rate

STUDY ID: 193
STUDY NO: 193ECG
ABBR: HR

SEX: MALE

UNITS: bpm

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

PERIOD(s): Pretest Week 13 Week 26

Group: 1-M : 0 mg base/kg/day

MEAN	105	123	119
SD	19.2	17.8	18.0
N	8	8	4

Group: 2-M : 0.1 mg base/kg/day

MEAN	107	129	123
SD	29.8	27.2	24.5
N	8	8	4

Group: 3-M : 0.3 mg base/kg/day

MEAN	97	121	128
SD	21.2	26.1	7.3
N	8	8	4

Group: 4-M : 1.0 mg base/kg/day

MEAN	123	134	126
SD	16.8	9.8	25.0
N	8	8	4

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

SUMMARY REPORT
TEST: P Wave Duration

STUDY ID: 193
STUDY NO: 193ECG
ABBR: P

SEX: MALE

UNITS: ms

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

PERIOD(s): Pretest Week 13 Week 26

Group: 1-M : 0 mg base/kg/day

MEAN	42	43	46
SD	5.4	5.3	5.2
N	8	8	4

Group: 2-M : 0.1 mg base/kg/day

MEAN	41	40	38
SD	5.0	4.2	5.1
N	8	8	4

Group: 3-M : 0.3 mg base/kg/day

MEAN	42	46	44
SD	4.2	5.5	7.6
N	8	8	4

Group: 4-M : 1.0 mg base/kg/day

MEAN	42	44	43
SD	2.8	5.7	3.1
N	8	8	4

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

SUMMARY REPORT
TEST: PR Interval

STUDY ID: 193
STUDY NO: 193ECG
ABBR: PR

SEX: MALE

UNITS: ms

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

PERIOD(s): Pretest Week 13 Week 26

Group: 1-M : 0 mg base/kg/day

MEAN	98	96	94
SD	9.7	11.6	12.1
N	8	8	4

Group: 2-M : 0.1 mg base/kg/day

MEAN	96	92	94
SD	10.8	7.0	12.0
N	8	8	4

Group: 3-M : 0.3 mg base/kg/day

MEAN	98	97	99
SD	7.2	5.5	8.2
N	8	8	4

Group: 4-M : 1.0 mg base/kg/day

MEAN	95	89	93
SD	6.3	6.7	13.1
N	8	8	4

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

SUMMARY REPORT
TEST: QRS Interval

STUDY ID: 193
STUDY NO: 193ECG
ABBR: QRS

SEX: MALE

UNITS: ms

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

PERIOD(s): Pretest Week 13 Week 26

Group: 1-M : 0 mg base/kg/day

MEAN	41	40	43
SD	2.1	1.6	1.7
N	8	8	4

Group: 2-M : 0.1 mg base/kg/day

MEAN	38	40	43
SD	3.2	1.2	2.6
N	8	8	4

Group: 3-M : 0.3 mg base/kg/day

MEAN	41	42	45
SD	4.6	4.8	5.2
N	8	8	4

Group: 4-M : 1.0 mg base/kg/day

MEAN	42	43	45
SD	2.4	2.5	2.4
N	8	8	4

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

SUMMARY REPORT
TEST: QT Interval

STUDY ID: 193
STUDY NO: 193ECG
ABBR: QT

SEX: MALE

UNITS: ms

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

PERIOD(s): Pretest Week 13 Week 26

Group: 1-M : 0 mg base/kg/day

MEAN	205	187	185
SD	18.8	18.3	5.0
N	8	8	4

Group: 2-M : 0.1 mg base/kg/day

MEAN	205	180	185
SD	18.5	15.4	18.7
N	8	8	4

Group: 3-M : 0.3 mg base/kg/day

MEAN	213	188	183
SD	17.8	24.5	12.3
N	8	8	4

Group: 4-M : 1.0 mg base/kg/day

MEAN	194	186	188
SD	14.4	13.7	21.3
N	8	8	4

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Heart Rate

STUDY ID: 193
STUDY NO: 193ECG
ABBR: HR

SEX: MALE

UNITS: bpm

Animal ID Pretest Week 13 Week 26

GROUP: 1-M:0 mg base/kg/day

8656	96	111	--
8687	89	106	--
8669	127	131	--
8673	139	134	--
8667	90	135	95
8654	86	95	136
8680	108	149	129
8676	108	121	116

MEAN	105	123	119
SD	19.2	17.8	18.0
N	8	8	4

GROUP: 2-M:0.1 mg base/kg/day

8685	120	157	--
8663	74	96	--
8686	84	108	--
8665	82	124	109
8666	138	129	159
8655	137	134	119
8659	78	109	106
8677	140	178	--

MEAN	107	129	123
SD	29.8	27.2	24.5
N	8	8	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Heart Rate

STUDY ID: 193
STUDY NO: 193ECG
ABBR: HR

SEX: MALE

UNITS: bpm

Animal ID Pretest Week 13 Week 26

GROUP: 3-M:0.3 mg base/kg/day

8674	102	153	127
8653	75	81	--
8660	81	144	--
8668	68	94	--
8682	94	115	118
8684	120	142	--
8662	121	105	133
8688	118	133	134

MEAN	97	121	128
SD	21.2	26.1	7.3
N	8	8	4

GROUP: 4-M:1.0 mg base/kg/day

8661	128	125	--
8670	96	128	--
8681	124	138	--
8664	127	123	--
8675	108	140	96
8683	125	146	156
8658	154	148	132
8652	118	127	120

MEAN	123	134	126
SD	16.8	9.8	25.0
N	8	8	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: P Wave Duration

STUDY ID: 193
STUDY NO: 193ECG
ABBR: P

SEX: MALE

UNITS: ms

Animal ID Pretest Week 13 Week 26

GROUP: 1-M:0 mg base/kg/day

8656	46	43	--
8687	40	41	--
8669	36	36	--
8673	42	40	--
8667	37	53	47
8654	39	40	50
8680	51	42	38
8676	48	48	47

MEAN	42	43	46
SD	5.4	5.3	5.2
N	8	8	4

GROUP: 2-M:0.1 mg base/kg/day

8685	39	33	--
8663	35	43	--
8686	49	46	--
8665	38	39	41
8666	43	35	35
8655	43	42	44
8659	35	41	33
8677	45	41	--

MEAN	41	40	38
SD	5.0	4.2	5.1
N	8	8	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: P Wave Duration

STUDY ID: 193
STUDY NO: 193ECG
ABBR: P

SEX: MALE

UNITS: ms

Animal ID Pretest Week 13 Week 26

GROUP: 3-M:0.3 mg base/kg/day

8674	41	42	41
8653	45	50	--
8660	41	43	--
8668	39	41	--
8682	38	39	34
8684	40	54	--
8662	41	45	48
8688	51	52	51

MEAN	42	46	44
SD	4.2	5.5	7.6
N	8	8	4

GROUP: 4-M:1.0 mg base/kg/day

8661	41	50	--
8670	38	35	--
8681	46	46	--
8664	45	51	--
8675	39	37	46
8683	42	44	39
8658	43	46	43
8652	40	45	45

MEAN	42	44	43
SD	2.8	5.7	3.1
N	8	8	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: PR Interval

STUDY ID: 193
STUDY NO: 193ECG
ABBR: PR

SEX: MALE

UNITS: ms

Animal ID Pretest Week 13 Week 26

GROUP: 1-M:0 mg base/kg/day

8656	108	110	--
8687	101	106	--
8669	84	80	--
8673	99	103	--
8667	93	99	98
8654	105	93	102
8680	107	97	100
8676	84	78	76

MEAN	98	96	94
SD	9.7	11.6	12.1
N	8	8	4

GROUP: 2-M:0.1 mg base/kg/day

8685	90	82	--
8663	97	97	--
8686	103	101	--
8665	84	86	87
8666	115	92	110
8655	102	99	96
8659	82	91	83
8677	96	85	--

MEAN	96	92	94
SD	10.8	7.0	12.0
N	8	8	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: PR Interval

STUDY ID: 193
STUDY NO: 193ECG
ABBR: PR

SEX: MALE

UNITS: ms

Animal ID Pretest Week 13 Week 26

GROUP: 3-M:0.3 mg base/kg/day

8674	102	93	101
8653	94	98	--
8660	88	92	--
8668	103	97	--
8682	92	91	90
8684	92	108	--
8662	102	100	95
8688	109	99	109

MEAN	98	97	99
SD	7.2	5.5	8.2
N	8	8	4

GROUP: 4-M:1.0 mg base/kg/day

8661	93	99	--
8670	100	85	--
8681	101	94	--
8664	94	88	--
8675	93	83	93
8683	86	78	77
8658	87	92	94
8652	103	91	109

MEAN	95	89	93
SD	6.3	6.7	13.1
N	8	8	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: QRS Interval

STUDY ID: 193
STUDY NO: 193ECG
ABBR: QRS

SEX: MALE

UNITS: ms

Animal ID Pretest Week 13 Week 26

GROUP: 1-M:0 mg base/kg/day

8656	43	40	--
8687	37	42	--
8669	40	38	--
8673	42	42	--
8667	40	38	42
8654	43	39	42
8680	43	40	41
8676	40	40	45

MEAN	41	40	43
SD	2.1	1.6	1.7
N	8	8	4

GROUP: 2-M:0.1 mg base/kg/day

8685	33	40	--
8663	36	38	--
8686	44	41	--
8665	39	38	46
8666	39	39	44
8655	39	39	42
8659	37	41	40
8677	40	40	--

MEAN	38	40	43
SD	3.2	1.2	2.6
N	8	8	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: QRS Interval

STUDY ID: 193
STUDY NO: 193ECG
ABBR: QRS

SEX: MALE

UNITS: ms

Animal ID Pretest Week 13 Week 26

GROUP: 3-M:0.3 mg base/kg/day

8674	41	44	41
8653	44	40	--
8660	39	39	--
8668	40	38	--
8682	43	38	41
8684	37	38	--
8662	34	46	44
8688	49	51	52

MEAN	41	42	45
SD	4.6	4.8	5.2
N	8	8	4

GROUP: 4-M:1.0 mg base/kg/day

8661	43	46	--
8670	44	45	--
8681	43	41	--
8664	41	44	--
8675	45	43	48
8683	39	42	45
8658	41	43	43
8652	38	38	43

MEAN	42	43	45
SD	2.4	2.5	2.4
N	8	8	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: QT Interval

STUDY ID: 193
STUDY NO: 193ECG
ABBR: QT

SEX: MALE

UNITS: ms

Animal ID Pretest Week 13 Week 26

GROUP: 1-M:0 mg base/kg/day

8656	221	194	--
8687	215	188	--
8669	187	164	--
8673	208	205	--
8667	187	183	180
8654	224	218	192
8680	175	166	185
8676	219	181	184

MEAN	205	187	185
SD	18.8	18.3	5.0
N	8	8	4

GROUP: 2-M:0.1 mg base/kg/day

8685	195	158	--
8663	234	201	--
8686	208	191	--
8665	199	175	182
8666	171	170	161
8655	215	190	190
8659	217	192	206
8677	202	164	--

MEAN	205	180	185
SD	18.5	15.4	18.7
N	8	8	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: QT Interval

STUDY ID: 193
STUDY NO: 193ECG
ABBR: QT

SEX: MALE

UNITS: ms

Animal ID Pretest Week 13 Week 26

GROUP: 3-M:0.3 mg base/kg/day

8674	205	167	168
8653	244	239	--
8660	223	177	--
8668	227	181	--
8682	202	188	178
8684	201	159	--
8662	217	200	189
8688	188	191	196

MEAN	213	188	183
SD	17.8	24.5	12.3
N	8	8	4

GROUP: 4-M:1.0 mg base/kg/day

8661	206	192	--
8670	210	189	--
8681	200	194	--
8664	198	210	--
8675	179	170	217
8683	167	168	168
8658	200	182	188
8652	190	180	177

MEAN	194	186	188
SD	14.4	13.7	21.3
N	8	8	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

SUMMARY REPORT
TEST: Heart Rate

STUDY ID: 193
STUDY NO: 193ECG
ABBR: HR

SEX: FEMALE

UNITS: bpm

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

PERIOD(s): Pretest Week 13 Week 26

Group: 1-F : 0 mg base/kg/day

MEAN	115	136	114
SD	21.5	30.6	21.8
N	8	8	4

Group: 2-F : 0.1 mg base/kg/day

MEAN	98	119	126
SD	25.2	11.9	17.0
N	8	8	4

Group: 3-F : 0.3 mg base/kg/day

MEAN	114	118	138
SD	20.4	24.9	15.4
N	8	8	4

Group: 4-F : 1.0 mg base/kg/day

MEAN	120	126	120
SD	32.6	31.5	38.4
N	8	8	4

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

SUMMARY REPORT
TEST: P Wave Duration

STUDY ID: 193
STUDY NO: 193ECG
ABBR: P

SEX: FEMALE

UNITS: ms

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

PERIOD(s): Pretest Week 13 Week 26

Group: 1-F : 0 mg base/kg/day

MEAN	41	43	41
SD	2.4	5.6	3.2
N	8	8	4

Group: 2-F : 0.1 mg base/kg/day

MEAN	43	43	44
SD	5.1	6.6	4.2
N	8	8	4

Group: 3-F : 0.3 mg base/kg/day

MEAN	44	42	41
SD	6.2	3.8	5.9
N	8	8	4

Group: 4-F : 1.0 mg base/kg/day

MEAN	44	43	43
SD	6.4	6.7	5.6
N	8	8	4

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

SUMMARY REPORT
TEST: PR Interval

STUDY ID: 193
STUDY NO: 193ECG
ABBR: PR

SEX: FEMALE

UNITS: ms

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

PERIOD(s): Pretest Week 13 Week 26

Group: 1-F : 0 mg base/kg/day

MEAN	102	96	105
SD	9.4	10.7	9.9
N	8	8	4

Group: 2-F : 0.1 mg base/kg/day

MEAN	99	99	98
SD	5.6	6.4	5.9
N	8	8	4

Group: 3-F : 0.3 mg base/kg/day

MEAN	106	96	96
SD	8.3	8.9	13.4
N	8	8	4

Group: 4-F : 1.0 mg base/kg/day

MEAN	107	99	106
SD	14.8	10.2	11.1
N	8	8	4

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

SUMMARY REPORT
TEST: QRS Interval

STUDY ID: 193
STUDY NO: 193ECG
ABBR: QRS

SEX: FEMALE

UNITS: ms

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

PERIOD(s): Pretest Week 13 Week 26

Group: 1-F : 0 mg base/kg/day

MEAN	40	41	42
SD	2.2	2.8	2.6
N	8	8	4

Group: 2-F : 0.1 mg base/kg/day

MEAN	39	41	42
SD	1.8	3.2	1.8
N	8	8	4

Group: 3-F : 0.3 mg base/kg/day

MEAN	40	40	40
SD	3.5	4.5	2.9
N	8	8	4

Group: 4-F : 1.0 mg base/kg/day

MEAN	41	41	47
SD	4.0	3.5	5.8
N	8	8	4

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

SUMMARY REPORT
TEST: QT Interval

STUDY ID: 193
STUDY NO: 193ECG
ABBR: QT

SEX: FEMALE

UNITS: ms

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

PERIOD(s): Pretest Week 13 Week 26

Group: 1-F : 0 mg base/kg/day

MEAN	188	193	201
SD	46.2	28.2	11.2
N	8	8	4

Group: 2-F : 0.1 mg base/kg/day

MEAN	212	186	181
SD	25.8	17.9	17.3
N	8	8	4

Group: 3-F : 0.3 mg base/kg/day

MEAN	194	186	179
SD	19.2	20.7	12.8
N	8	8	4

Group: 4-F : 1.0 mg base/kg/day

MEAN	194	184	199
SD	16.4	13.8	22.4
N	8	8	4

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Heart Rate

STUDY ID: 193
STUDY NO: 193ECG
ABBR: HR

SEX: FEMALE

UNITS: bpm

Animal ID Pretest Week 13 Week 26

GROUP: 1-F:0 mg base/kg/day

8721	116	183	--
8712	80	90	--
8710	94	119	--
8723	118	139	--
8705	138	135	130
8700	101	104	105
8699	134	161	87
8690	137	153	133
MEAN	115	136	114
SD	21.5	30.6	21.8
N	8	8	4

GROUP: 2-F:0.1 mg base/kg/day

8717	119	110	--
8703	142	141	--
8713	99	106	--
8693	109	108	--
8695	70	112	117
8709	66	126	148
8715	93	124	129
8697	87	122	109
MEAN	98	119	126
SD	25.2	11.9	17.0
N	8	8	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Heart Rate

STUDY ID: 193
STUDY NO: 193ECG
ABBR: HR

SEX: FEMALE

UNITS: bpm

Animal ID Pretest Week 13 Week 26

GROUP: 3-F:0.3 mg base/kg/day

8692	96	79	--
8718	138	133	--
8706	130	126	--
8714	121	144	--
8701	123	139	136
8702	75	92	133
8720	121	136	160
8704	106	98	124

MEAN	114	118	138
SD	20.4	24.9	15.4
N	8	8	4

GROUP: 4-F:1.0 mg base/kg/day

8696	113	84	--
8719	93	134	--
8711	96	90	--
8716	194	178	--
8725	133	144	148
8707	114	135	141
8689	115	102	64
8722	100	137	128

MEAN	120	126	120
SD	32.6	31.5	38.4
N	8	8	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: P Wave Duration

STUDY ID: 193
STUDY NO: 193ECG
ABBR: P

SEX: FEMALE

UNITS: ms

Animal ID Pretest Week 13 Week 26

GROUP: 1-F:0 mg base/kg/day

8721	38	38	--
8712	40	44	--
8710	42	43	--
8723	42	44	--
8705	45	38	39
8700	42	53	42
8699	42	45	45
8690	38	35	38

MEAN	41	43	41
SD	2.4	5.6	3.2
N	8	8	4

GROUP: 2-F:0.1 mg base/kg/day

8717	37	35	--
8703	40	43	--
8713	47	41	--
8693	40	38	--
8695	40	40	38
8709	53	57	48
8715	44	45	45
8697	42	43	44

MEAN	43	43	44
SD	5.1	6.6	4.2
N	8	8	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: P Wave Duration

STUDY ID: 193
STUDY NO: 193ECG
ABBR: P

SEX: FEMALE

UNITS: ms

Animal ID Pretest Week 13 Week 26

GROUP: 3-F:0.3 mg base/kg/day

8692	39	42	--
8718	49	43	--
8706	52	45	--
8714	51	33	--
8701	40	42	35
8702	35	45	39
8720	42	41	42
8704	42	42	49

MEAN	44	42	41
SD	6.2	3.8	5.9
N	8	8	4

GROUP: 4-F:1.0 mg base/kg/day

8696	40	36	--
8719	50	42	--
8711	41	41	--
8716	37	56	--
8725	45	49	50
8707	40	39	40
8689	56	41	43
8722	40	37	37

MEAN	44	43	43
SD	6.4	6.7	5.6
N	8	8	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: PR Interval

STUDY ID: 193
STUDY NO: 193ECG
ABBR: PR

SEX: FEMALE

UNITS: ms

Animal ID Pretest Week 13 Week 26

GROUP: 1-F:0 mg base/kg/day

8721	90	84	--
8712	99	108	--
8710	93	86	--
8723	108	95	--
8705	101	100	104
8700	119	114	117
8699	108	92	107
8690	97	89	93

MEAN	102	96	105
SD	9.4	10.7	9.9
N	8	8	4

GROUP: 2-F:0.1 mg base/kg/day

8717	101	94	--
8703	98	95	--
8713	97	101	--
8693	103	108	--
8695	87	92	98
8709	100	103	100
8715	103	92	90
8697	105	106	104

MEAN	99	99	98
SD	5.6	6.4	5.9
N	8	8	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: PR Interval

STUDY ID: 193
STUDY NO: 193ECG
ABBR: PR

SEX: FEMALE

UNITS: ms

Animal ID Pretest Week 13 Week 26

GROUP: 3-F:0.3 mg base/kg/day

8692	95	87	--
8718	103	97	--
8706	121	106	--
8714	108	93	--
8701	100	85	84
8702	101	92	84
8720	107	97	105
8704	114	111	109

MEAN	106	96	96
SD	8.3	8.9	13.4
N	8	8	4

GROUP: 4-F:1.0 mg base/kg/day

8696	109	108	--
8719	104	84	--
8711	127	109	--
8716	80	93	--
8725	121	113	122
8707	107	96	102
8689	113	99	102
8722	94	90	97

MEAN	107	99	106
SD	14.8	10.2	11.1
N	8	8	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: QRS Interval

STUDY ID: 193
STUDY NO: 193ECG
ABBR: QRS

SEX: FEMALE

UNITS: ms

Animal ID Pretest Week 13 Week 26

GROUP: 1-F:0 mg base/kg/day

8721	38	40	--
8712	39	41	--
8710	40	40	--
8723	45	41	--
8705	40	47	46
8700	39	38	42
8699	41	40	40
8690	39	38	41

MEAN	40	41	42
SD	2.2	2.8	2.6
N	8	8	4

GROUP: 2-F:0.1 mg base/kg/day

8717	40	43	--
8703	39	42	--
8713	38	47	--
8693	38	38	--
8695	38	38	41
8709	40	38	40
8715	38	39	44
8697	43	42	43

MEAN	39	41	42
SD	1.8	3.2	1.8
N	8	8	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

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INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: QRS Interval

STUDY ID: 193
STUDY NO: 193ECG
ABBR: QRS

SEX: FEMALE

UNITS: ms

Animal ID Pretest Week 13 Week 26

GROUP: 3-F:0.3 mg base/kg/day

8692	35	35	--
8718	40	41	--
8706	47	50	--
8714	40	38	--
8701	38	40	42
8702	39	38	37
8720	38	37	38
8704	41	41	43

MEAN	40	40	40
SD	3.5	4.5	2.9
N	8	8	4

GROUP: 4-F:1.0 mg base/kg/day

8696	37	40	--
8719	39	41	--
8711	40	44	--
8716	37	38	--
8725	38	37	45
8707	47	48	42
8689	45	40	55
8722	45	42	44

MEAN	41	41	47
SD	4.0	3.5	5.8
N	8	8	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

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INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: QT Interval

STUDY ID: 193
STUDY NO: 193ECG
ABBR: QT

SEX: FEMALE

UNITS: ms

Animal ID Pretest Week 13 Week 26

GROUP: 1-F:0 mg base/kg/day

8721	170	152	--
8712	220	224	--
8710	219	183	--
8723	214	195	--
8705	82	179	203
8700	192	242	196
8699	214	180	216
8690	189	186	190

MEAN	188	193	201
SD	46.2	28.2	11.2
N	8	8	4

GROUP: 2-F:0.1 mg base/kg/day

8717	188	180	--
8703	185	175	--
8713	227	207	--
8693	206	213	--
8695	245	192	196
8709	245	171	165
8715	182	161	167
8697	215	191	196

MEAN	212	186	181
SD	25.8	17.9	17.3
N	8	8	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

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INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: QT Interval

STUDY ID: 193
STUDY NO: 193ECG
ABBR: QT

SEX: FEMALE

UNITS: ms

Animal ID Pretest Week 13 Week 26

GROUP: 3-F:0.3 mg base/kg/day

8692	210	195	--
8718	167	174	--
8706	171	175	--
8714	201	168	--
8701	181	159	172
8702	206	205	180
8720	199	188	168
8704	220	221	197

MEAN	194	186	179
SD	19.2	20.7	12.8
N	8	8	4

GROUP: 4-F:1.0 mg base/kg/day

8696	208	204	--
8719	200	183	--
8711	200	198	--
8716	155	169	--
8725	190	178	188
8707	195	169	184
8689	202	197	232
8722	199	175	191

MEAN	194	184	199
SD	16.4	13.8	22.4
N	8	8	4

(--) - Data Unavailable

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APPENDIX J
Ophthalmology Report

ANIMAL EYE ASSOCIATES

2845 SOUTH HARLEM • BERWYN, ILLINOIS 60402 • (708) 749-4200
372 SOUTH MILWAUKEE AVE. • WHEELING, ILLINOIS 60090 • (708) 215-3933

DRAFT

SAMUEL J. VAINISI, DVM
Diplomate American College
of Veterinary Ophthalmologists

GRETCHEN M. SCHMIDT, DVM
Diplomate American College
of Veterinary Ophthalmologists

April 11, 1996

OPHTHALMIC REPORT

UIC/TRL Study No. 193

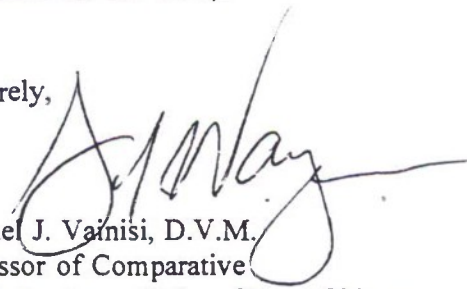
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

During Week -3 (August 22, 1995), a sufficient number of beagle dogs were given ophthalmic examinations by indirect ophthalmoscopy to result in thirty-two males and thirty-two females which were within normal limits.

During Week 13 (December 05, 1995), all animals which were used in the above-referenced study were re-examined. All dogs appeared similar (no lesions) to their pretest examinations performed on August 22, 1995.

During Week 26 (March 5, 1996), the remaining thirty-two animals used in the above-referenced study were re-examined. All dogs appeared similar (no lesions) to their examinations during Week -3 (August 22, 1995) and Week 13 (December 05, 1995).

Sincerely,



Samuel J. Vainisi, D.V.M.
Professor of Comparative
Ophthalmology, Univ. of IL at Chicago

Diplomate, American College of
Veterinary Ophthalmologists

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

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Ophthalmic Examinations (Males)

Dose (mg base/kg/day)	Animal Number	Week -3		Week 13		Week 26	
		R.E.	L.E.	R.E.	L.E.	R.E.	L.E.
0	8654	WNL	WNL	WNL	WNL	WNL	WNL
	8655	WNL	WNL	WNL	WNL	-	-
	8652	WNL	WNL	WNL	WNL	WNL	WNL
	8669	WNL	WNL	WNL	WNL	-	-
	8673	WNL	WNL	WNL	WNL	-	-
	8676	WNL	WNL	WNL	WNL	WNL	WNL
	8680	WNL	WNL	WNL	WNL	WNL	WNL
	8687	WNL	WNL	WNL	WNL	-	-
0.1	8655	WNL	WNL	WNL	WNL	WNL	WNL
	8655	WNL	WNL	WNL	WNL	WNL	WNL
	8663	WNL	WNL	WNL	WNL	-	-
	8665	WNL	WNL	WNL	WNL	WNL	WNL
	8666	WNL	WNL	WNL	WNL	WNL	WNL
	8674	WNL	WNL	WNL	WNL	-	-
	8655	WNL	WNL	WNL	WNL	-	-
	8655	WNL	WNL	WNL	WNL	-	-
0.3	8655	WNL	WNL	WNL	WNL	-	-
	8660	WNL	WNL	WNL	WNL	-	-
	8658	WNL	WNL	WNL	WNL	WNL	WNL
	8688	WNL	WNL	WNL	WNL	-	-
	8674	WNL	WNL	WNL	WNL	WNL	WNL
	8688	WNL	WNL	WNL	WNL	WNL	WNL
	8684	WNL	WNL	WNL	WNL	-	-
	8688	WNL	WNL	WNL	WNL	WNL	WNL
1.0	8652	WNL	WNL	WNL	WNL	WNL	WNL
	8688	WNL	WNL	WNL	WNL	WNL	WNL
	8658	WNL	WNL	WNL	WNL	-	-
	8664	WNL	WNL	WNL	WNL	-	-
	8674	WNL	WNL	WNL	WNL	-	-
	8675	WNL	WNL	WNL	WNL	WNL	WNL
	8681	WNL	WNL	WNL	WNL	-	-
	8683	WNL	WNL	WNL	WNL	WNL	WNL

- = Animal previously sacrificed
R.E. = Right Eye
L.E. = Left Eye
WNL = Within Normal Limits

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

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Ophthalmic Examinations (Females)

Dose (mg base/kg/day)	Animal Number	Week -3		Week 13		Week 26	
		R.E.	L.E.	R.E.	L.E.	R.E.	L.E.
0	8690	WNL	WNL	WNL	WNL	WNL	WNL
	8699	WNL	WNL	WNL	WNL	WNL	WNL
	8700	WNL	WNL	WNL	WNL	WNL	WNL
	8709	WNL	WNL	WNL	WNL	WNL	WNL
	8716	WNL	WNL	WNL	WNL	-	-
	8712	WNL	WNL	WNL	WNL	-	-
	8721	WNL	WNL	WNL	WNL	-	-
	8723	WNL	WNL	WNL	WNL	-	-
0.1	8699	WNL	WNL	WNL	WNL	-	-
	8689	WNL	WNL	WNL	WNL	WNL	WNL
	8697	WNL	WNL	WNL	WNL	WNL	WNL
	8709	WNL	WNL	WNL	WNL	-	-
	8709	WNL	WNL	WNL	WNL	WNL	WNL
	8713	WNL	WNL	WNL	WNL	-	-
	8715	WNL	WNL	WNL	WNL	WNL	WNL
	8712	WNL	WNL	WNL	WNL	-	-
0.3	8692	WNL	WNL	WNL	WNL	-	-
	8711	WNL	WNL	WNL	WNL	WNL	WNL
	8702	WNL	WNL	WNL	WNL	WNL	WNL
	8704	WNL	WNL	WNL	WNL	WNL	WNL
	8709	WNL	WNL	WNL	WNL	-	-
	8716	WNL	WNL	WNL	WNL	-	-
	8716	WNL	WNL	WNL	WNL	-	-
	8709	WNL	WNL	WNL	WNL	WNL	WNL
1.0	8689	WNL	WNL	WNL	WNL	WNL	WNL
	8696	WNL	WNL	WNL	WNL	-	-
	8707	WNL	WNL	WNL	WNL	WNL	WNL
	8711	WNL	WNL	WNL	WNL	-	-
	8716	WNL	WNL	WNL	WNL	-	-
	8719	WNL	WNL	WNL	WNL	-	-
	8722	WNL	WNL	WNL	WNL	WNL	WNL
	8725	WNL	WNL	WNL	WNL	WNL	WNL

- = Animal previously sacrificed
R.E. = Right Eye
L.E. = Left Eye
WNL = Within Normal Limits

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APPENDIX K
Individual Organ Weights

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 193
SEX: MALE

GROUP: 1-M - 0 mg base/kg/day
ALL FATES DAYS: 92-93 ALL BALANCES

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ANIMAL ID: BALANCE NO.:	8656	8669	8673	8687
BODY WEIGHT (G)	10.8	12.2	12.3	11.2
Adrenal Glands (G)	1.30	1.43	1.33	1.61
% BRAIN WEIGHT	1.70	1.88	1.83	2.34
Brain (G)	76.61	76.09	72.85	68.93
Heart (G)	84.70	88.35	106.81	87.98
% BRAIN WEIGHT	110.56	116.11	146.62	127.64
Kidneys (G)	57.23	45.77	50.62	41.53
% BRAIN WEIGHT	74.70	60.15	69.49	60.25
Liver (G)	266.60	248.75	297.14	250.22
% BRAIN WEIGHT	348.00	326.92	407.88	363.01
Spleen (G)	46.10	37.87	30.33	44.79
% BRAIN WEIGHT	60.17	49.77	41.63	64.98
Testes (G)	14.50	16.32	13.85	15.22
% BRAIN WEIGHT	18.93	21.45	19.01	22.08
Thyroid + Parathyroids (G)	1.12	1.12	0.88	0.89
% BRAIN WEIGHT	1.46	1.47	1.21	1.29

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 193
SEX: MALE

GROUP: 2-M - 0.1 mg base/kg/day
ALL FATES DAYS: 92-93 ALL BALANCES

DRAFT

ANIMAL ID: BALANCE NO.:	8663	8677	8685	8686
BODY WEIGHT (G)	12.6	14.0	10.5	11.4
Adrenal Glands (G)	1.24	1.11	1.73	1.33
% BRAIN WEIGHT	1.65	1.47	2.12	1.67
Brain (G)	75.08	75.68	81.71	79.46
Heart (G)	88.74	79.23	84.52	101.62
% BRAIN WEIGHT	118.19	104.69	103.44	127.89
Kidneys (G)	45.15	62.93	56.36	51.33
% BRAIN WEIGHT	60.14	83.15	68.98	64.60
Liver (G)	292.02	345.40	272.59	295.42
% BRAIN WEIGHT	388.95	456.40	333.61	371.78
Spleen (G)	25.88	33.55	35.26	32.21
% BRAIN WEIGHT	34.47	44.33	43.15	40.54
Testes (G)	14.35	13.28	17.96	12.74
% BRAIN WEIGHT	19.11	17.55	21.98	16.03
Thyroid + Parathyroids (G)	1.16	1.30	0.94	1.11
% BRAIN WEIGHT	1.55	1.72	1.15	1.40

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 193
SEX: MALE

GROUP: 3-M - 0.3 mg base/kg/day
ALL FATES DAYS: 92-93 ALL BALANCES

DRAFT

ANIMAL ID: BALANCE NO.:	8653	8660	8668	8684
BODY WEIGHT (G)	9.0	12.2	12.6	11.2
Adrenal Glands (G)	1.45	1.51	1.47	1.36
% BRAIN WEIGHT	1.75	1.88	1.72	1.61
Brain (G)	83.04	80.16	85.48	84.64
Heart (G)	87.18	90.61	99.99	101.44
% BRAIN WEIGHT	104.99	113.04	116.97	119.85
Kidneys (G)	41.61	45.35	55.54	51.20
% BRAIN WEIGHT	50.11	56.57	64.97	60.49
Liver (G)	264.79	343.63	364.65	278.17
% BRAIN WEIGHT	318.87	428.68	426.59	328.65
Spleen (G)	26.74	35.56	48.78	50.24
% BRAIN WEIGHT	32.20	44.36	57.07	59.36
Testes (G)	12.50	16.40	14.67	14.55
% BRAIN WEIGHT	15.05	20.46	17.16	17.19
Thyroid + Parathyroids (G)	0.85	1.35	1.17	1.01
% BRAIN WEIGHT	1.02	1.68	1.37	1.19

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 193
SEX: MALE

GROUP: 4-M - 1.0 mg base/kg/day
ALL FATES DAYS: 92-93 ALL BALANCES

DRAFT

ANIMAL ID: BALANCE NO.:	8661	8664	8670	8681
BODY WEIGHT (G)	10.6	11.0	9.8	12.1
Adrenal Glands (G)	1.08	1.16	1.46	1.44
% BRAIN WEIGHT	1.26	1.39	1.84	1.68
Brain (G)	85.67	83.35	79.24	85.92
Heart (G)	94.77	91.34	82.94	94.02
% BRAIN WEIGHT	110.62	109.59	104.67	109.43
Kidneys (G)	44.43	50.68	51.38	57.83
% BRAIN WEIGHT	51.86	60.80	64.84	67.31
Liver (G)	321.42	355.20	343.21	333.48
% BRAIN WEIGHT	375.18	426.15	433.13	388.13
Spleen (G)	49.22	47.92	19.44	36.72
% BRAIN WEIGHT	57.45	57.49	24.53	42.74
Testes (G)	16.28	11.35	11.55	14.27
% BRAIN WEIGHT	19.00	13.62	14.58	16.61
Thyroid + Parathyroids (G)	1.05	1.08	0.88	1.36
% BRAIN WEIGHT	1.23	1.30	1.11	1.58

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 193
SEX: MALE

GROUP: 1-M - 0 mg base/kg/day
ALL FATES DAYS: 183-184 ALL BALANCES

DRAFT

ANIMAL ID: BALANCE NO.:	8654 612026	8667 612026	8676 612026	8680 612026
BODY WEIGHT (G)	10.9	10.8	16.1	13.4
Adrenal Glands (G)	1.54	1.20	1.37	2.47
% BRAIN WEIGHT	1.59	1.55	1.58	3.03
Brain (G)	96.94	77.64	86.50	81.46
Heart (G)	86.14	88.55	117.81	102.22
% BRAIN WEIGHT	88.86	114.05	136.20	125.48
Kidneys (G)	47.21	55.28	68.45	62.91
% BRAIN WEIGHT	48.70	71.20	79.13	77.23
Liver (G)	289.30	225.50	294.25	256.95
% BRAIN WEIGHT	298.43	290.44	340.17	315.43
Spleen (G)	27.34	34.34	42.03	44.24
% BRAIN WEIGHT	28.20	44.23	48.59	54.31
Testes (G)	14.08	17.77	18.86	19.40
% BRAIN WEIGHT	14.52	22.89	21.80	23.82
Thyroid + Parathyroids (G)	0.98	0.80	1.39	1.80
% BRAIN WEIGHT	1.01	1.03	1.61	2.21

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 193
SEX: MALE

GROUP: 2-M - 0.1 mg base/kg/day
ALL FATES DAYS: 183-184 ALL BALANCES

DRAFT

ANIMAL ID: BALANCE NO.:	8655 612026	8659 612026	8665 612026	8666 612026
BODY WEIGHT (G)	12.6	11.5	11.9	11.8
Adrenal Glands (G)	1.64	1.30	1.96	1.45
% BRAIN WEIGHT	1.84	1.62	2.56	1.75
Brain (G)	89.19	80.25	76.70	82.75
Heart (G)	108.03	95.90	100.04	100.57
% BRAIN WEIGHT	121.12	119.50	130.43	121.53
Kidneys (G)	68.50	55.86	49.01	53.40
% BRAIN WEIGHT	76.80	69.61	63.90	64.53
Liver (G)	300.53	278.15	245.41	243.39
% BRAIN WEIGHT	336.95	346.60	319.96	294.13
Spleen (G)	46.40	38.41	31.62	36.47
% BRAIN WEIGHT	52.02	47.86	41.23	44.07
Testes (G)	16.40	16.91	10.82	9.90
% BRAIN WEIGHT	18.39	21.07	14.11	11.96
Thyroid + Parathyroids (G)	1.00	1.27	0.92	1.37
% BRAIN WEIGHT	1.12	1.58	1.20	1.66

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 193
SEX: MALE

GROUP: 3-M - 0.3 mg base/kg/day
ALL FATES DAYS: 183-184 ALL BALANCES

DRAFT

ANIMAL ID: BALANCE NO.:	8662 612026	8674 612026	8682 612026	8688 612026
BODY WEIGHT (G)	10.9	11.0	9.3	14.0
Adrenal Glands (G)	1.53	1.06	1.25	1.23
% BRAIN WEIGHT	1.74	1.37	1.65	1.64
Brain (G)	87.77	77.32	75.60	75.15
Heart (G)	102.24	97.52	78.23	89.49
% BRAIN WEIGHT	116.49	126.13	103.48	119.08
Kidneys (G)	54.57	58.12	47.50	44.16
% BRAIN WEIGHT	62.17	75.17	62.83	58.76
Liver (G)	285.26	259.56	280.22	268.27
% BRAIN WEIGHT	325.01	335.70	370.66	356.98
Spleen (G)	23.91	22.38	39.26	69.66
% BRAIN WEIGHT	27.24	28.94	51.93	92.69
Testes (G)	14.83	14.10	14.59	13.76
% BRAIN WEIGHT	16.90	18.24	19.30	18.31
Thyroid + Parathyroids (G)	0.97	0.92	0.81	1.22
% BRAIN WEIGHT	1.11	1.19	1.07	1.62

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 193
SEX: MALE

GROUP: 4-M - 1.0 mg base/kg/day
ALL FATES DAYS: 183-184 ALL BALANCES

DRAFT

ANIMAL ID: BALANCE NO.:	8652 612026	8658 612026	8675 612026	8683 612026
BODY WEIGHT (G)	13.2	10.0	11.6	12.2
Adrenal Glands (G)	1.55	1.35	1.24	1.92
% BRAIN WEIGHT	1.82	1.69	1.55	2.19
Brain (G)	85.30	80.00	79.96	87.74
Heart (G)	110.37	82.20	100.24	96.74
% BRAIN WEIGHT	129.39	102.75	125.36	110.26
Kidneys (G)	55.67	50.50	62.11	50.70
% BRAIN WEIGHT	65.26	63.13	77.68	57.78
Liver (G)	350.79	302.87	294.81	309.86
% BRAIN WEIGHT	411.24	378.59	368.70	353.16
Spleen (G)	42.70	33.14	39.53	48.74
% BRAIN WEIGHT	50.06	41.43	49.44	55.55
Testes (G)	21.38	11.57	10.80	14.46
% BRAIN WEIGHT	25.06	14.46	13.51	16.48
Thyroid + Parathyroids (G)	1.14	1.22	1.10	1.23
% BRAIN WEIGHT	1.34	1.53	1.38	1.40

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 193
SEX: FEMALE

GROUP: 1-F - 0 mg base/kg/day
ALL FATES DAYS: 92-93 ALL BALANCES

DRAFT

ANIMAL ID: BALANCE NO.:	8710	8712	8721	8723
BODY WEIGHT (G)	11.2	9.9	8.9	11.0
Adrenal Glands (G)	2.14	1.11	1.09	1.62
% BRAIN WEIGHT	2.77	1.53	1.56	2.07
Brain (G)	77.13	72.48	70.06	78.26
Heart (G)	83.77	90.45	72.64	91.68
% BRAIN WEIGHT	108.61	124.79	103.68	117.15
Kidneys (G)	41.23	38.91	32.60	42.77
% BRAIN WEIGHT	53.46	53.68	46.53	54.65
Liver (G)	249.97	209.07	220.06	312.72
% BRAIN WEIGHT	324.09	288.45	314.10	399.59
Ovaries (G)	0.86	1.01	0.84	1.80
% BRAIN WEIGHT	1.12	1.39	1.20	2.30
Spleen (G)	40.56	20.80	23.40	38.94
% BRAIN WEIGHT	52.59	28.70	33.40	49.76
Thyroid + Parathyroids (G)	0.95	0.94	1.03	0.87
% BRAIN WEIGHT	1.23	1.30	1.47	1.11

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 193
SEX: FEMALE

GROUP: 2-F - 0.1 mg base/kg/day
ALL FATES DAYS: 92-93 ALL BALANCES

DRAFT

ANIMAL ID: BALANCE NO.:	8693	8703	8713	8717
BODY WEIGHT (G)	11.5	9.1	11.4	8.6
Adrenal Glands (G)	1.48	1.50	2.17	1.54
% BRAIN WEIGHT	1.96	2.21	2.90	2.11
Brain (G)	75.43	67.85	74.79	72.97
Heart (G)	79.77	70.66	97.44	83.15
% BRAIN WEIGHT	105.75	104.14	130.28	113.95
Kidneys (G)	44.40	38.13	49.52	37.04
% BRAIN WEIGHT	58.86	56.20	66.21	50.76
Liver (G)	301.96	233.31	308.97	229.18
% BRAIN WEIGHT	400.32	343.86	413.12	314.07
Ovaries (G)	2.46	0.67	2.79	0.69
% BRAIN WEIGHT	3.26	0.99	3.73	0.95
Spleen (G)	37.37	32.18	50.05	34.42
% BRAIN WEIGHT	49.54	47.43	66.92	47.17
Thyroid + Parathyroids (G)	1.00	0.76	1.04	0.77
% BRAIN WEIGHT	1.33	1.12	1.39	1.06

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 193
SEX: FEMALE

GROUP: 3-F - 0.3 mg base/kg/day
ALL FATES DAYS: 92-93 ALL BALANCES

DRAFT

ANIMAL ID: BALANCE NO.:	8692	8706	8714	8718
BODY WEIGHT (G)	8.1	10.3	12.2	9.7
Adrenal Glands (G)	1.03	1.58	1.56	1.17
% BRAIN WEIGHT	1.46	2.36	2.01	1.41
Brain (G)	70.41	66.93	77.53	82.85
Heart (G)	69.94	82.59	86.62	87.68
% BRAIN WEIGHT	99.33	123.40	111.72	105.83
Kidneys (G)	36.82	41.51	46.83	40.63
% BRAIN WEIGHT	52.29	62.02	60.40	49.04
Liver (G)	240.02	315.19	294.77	248.83
% BRAIN WEIGHT	340.89	470.92	380.20	300.34
Ovaries (G)	1.17	1.20	2.55	1.22
% BRAIN WEIGHT	1.66	1.79	3.29	1.47
Spleen (G)	28.02	48.76	53.28	47.16
% BRAIN WEIGHT	39.80	72.85	68.72	56.92
Thyroid + Parathyroids (G)	0.86	0.91	1.25	0.96
% BRAIN WEIGHT	1.22	1.36	1.61	1.16

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 193
SEX: FEMALE

GROUP: 4-F - 1.0 mg base/kg/day
ALL FATES DAYS: 92-93 ALL BALANCES

DRAFT

ANIMAL ID: BALANCE NO.:	8696	8711	8716	8719
BODY WEIGHT (G)	8.2	9.8	10.1	9.0
Adrenal Glands (G)	1.14	1.57	1.03	0.95
% BRAIN WEIGHT	1.37	2.25	1.32	1.26
Brain (G)	83.12	69.73	77.91	75.40
Heart (G)	68.98	87.40	83.47	70.68
% BRAIN WEIGHT	82.99	125.34	107.14	93.74
Kidneys (G)	41.78	44.56	39.13	41.94
% BRAIN WEIGHT	50.26	63.90	50.22	55.62
Liver (G)	250.78	298.79	322.44	264.19
% BRAIN WEIGHT	301.71	428.50	413.86	350.38
Ovaries (G)	0.80	0.85	1.34	1.25
% BRAIN WEIGHT	0.96	1.22	1.72	1.66
Spleen (G)	51.11	32.59	90.26	34.13
% BRAIN WEIGHT	61.49	46.74	115.85	45.27
Thyroid + Parathyroids (G)	1.10	0.83	0.66	0.85
% BRAIN WEIGHT	1.32	1.19	0.85	1.13

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 193
SEX: FEMALE

GROUP: 1-F - 0 mg base/kg/day
ALL FATES DAYS: 183-184 ALL BALANCES

DRAFT

ANIMAL ID:	8690	8699	8700	8705
BALANCE NO.:	2026	2026	2026	2026
BODY WEIGHT (G)	12.8	10.7	10.3	9.2
Adrenal Glands (G)	1.59	1.71	1.62	1.39
% BRAIN WEIGHT	2.03	2.11	2.07	1.98
Brain (G)	78.17	81.12	78.30	70.20
Heart (G)	73.70	84.07	81.63	74.86
% BRAIN WEIGHT	94.28	103.64	104.25	106.64
Kidneys (G)	41.13	34.06	45.39	32.76
% BRAIN WEIGHT	52.62	41.99	57.97	46.67
Liver (G)	293.09	202.01	246.18	219.77
% BRAIN WEIGHT	374.94	249.03	314.41	313.06
Ovaries (G)	1.28	0.90	1.78	1.83
% BRAIN WEIGHT	1.64	1.11	2.27	2.61
Spleen (G)	36.18	33.54	33.33	34.87
% BRAIN WEIGHT	46.28	41.35	42.57	49.67
Thyroid + Parathyroids (G)	1.22	0.95	0.93	0.84
% BRAIN WEIGHT	1.56	1.17	1.19	1.20

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 193
SEX: FEMALE

GROUP: 2-F - 0.1 mg base/kg/day
ALL FATES DAYS: 183-184 ALL BALANCES

DRAFT

ANIMAL ID:	8695	8697	8709	8715
BALANCE NO.:	2026	2026	2026	2026
BODY WEIGHT (G)	9.3	12.7	10.0	11.0
Adrenal Glands (G)	1.17	1.90	1.11	1.83
% BRAIN WEIGHT	1.59	2.68	1.45	2.46
Brain (G)	73.40	70.90	76.37	74.51
Heart (G)	66.78	89.90	94.09	90.63
% BRAIN WEIGHT	90.98	126.80	123.20	121.63
Kidneys (G)	30.07	37.96	36.93	37.59
% BRAIN WEIGHT	40.97	53.54	48.36	50.45
Liver (G)	186.64	241.32	276.18	207.19
% BRAIN WEIGHT	254.28	340.37	361.63	278.07
Ovaries (G)	0.80	1.24	1.24	0.97
% BRAIN WEIGHT	1.09	1.75	1.62	1.30
Spleen (G)	25.66	43.74	28.31	29.55
% BRAIN WEIGHT	34.96	61.69	37.07	39.66
Thyroid + Parathyroids (G)	0.82	0.88	1.04	0.76
% BRAIN WEIGHT	1.12	1.24	1.36	1.02

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 193
SEX: FEMALE

GROUP: 3-F - 0.3 mg base/kg/day
ALL FATES DAYS: 183-184 ALL BALANCES

DRAFT

ANIMAL ID: BALANCE NO.:	8701 2026	8702 2026	8704 2026	8720 2026
BODY WEIGHT (G)	9.0	8.1	11.4	10.3
Adrenal Glands (G)	1.44	2.33	1.55	1.20
% BRAIN WEIGHT	1.74	3.25	1.92	1.66
Brain (G)	82.65	71.74	80.87	72.19
Heart (G)	74.88	86.99	94.34	71.13
% BRAIN WEIGHT	90.60	121.26	116.66	98.53
Kidneys (G)	46.90	41.78	47.98	46.01
% BRAIN WEIGHT	56.75	58.24	59.33	63.73
Liver (G)	217.52	237.27	243.44	230.09
% BRAIN WEIGHT	263.18	330.74	301.03	318.73
Ovaries (G)	1.38	1.04	1.47	1.07
% BRAIN WEIGHT	1.67	1.45	1.82	1.48
Spleen (G)	31.67	24.53	38.00	30.86
% BRAIN WEIGHT	38.32	34.19	46.99	42.75
Thyroid + Parathyroids (G)	0.64	0.83	1.08	0.74
% BRAIN WEIGHT	0.77	1.16	1.34	1.03

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 193
SEX: FEMALE

GROUP: 4-F - 1.0 mg base/kg/day
ALL FATES DAYS: 183-184 ALL BALANCES

DRAFT

ANIMAL ID:	8689	8707	8722	8725
BALANCE NO.:	2026	2026	2026	2026
BODY WEIGHT (G)	9.9	10.6	9.8	8.3
Adrenal Glands (G)	2.39	1.50	1.06	1.51
% BRAIN WEIGHT	2.78	1.87	1.66	2.00
Brain (G)	86.08	80.25	63.75	75.54
Heart (G)	81.50	78.96	78.08	79.72
% BRAIN WEIGHT	94.68	98.39	122.48	105.53
Kidneys (G)	41.36	42.59	38.29	41.45
% BRAIN WEIGHT	48.05	53.07	60.06	54.87
Liver (G)	297.44	247.58	277.14	322.48
% BRAIN WEIGHT	345.54	308.51	434.73	426.90
Ovaries (G)	1.45	2.15	1.73	1.26
% BRAIN WEIGHT	1.68	2.68	2.71	1.67
Spleen (G)	31.27	50.63	32.40	24.51
% BRAIN WEIGHT	36.33	63.09	50.82	32.45
Thyroid + Parathyroids (G)	0.86	0.93	0.82	0.69
% BRAIN WEIGHT	1.00	1.16	1.29	0.91

DRAFT

APPENDIX L
Pathology Report

DRAFT PATHOLOGY REPORT FOR
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS
UIC/TRL STUDY NUMBER 193

PREPARED
BY
PATHOLOGY ASSOCIATES INTERNATIONAL
2201 WEST CAMPBELL PARK DRIVE, SUITE 327
CHICAGO, IL 60612

FOR
TOXICOLOGY RESEARCH LABORATORY (M/C 868)
DEPARTMENT OF PHARMACOLOGY
UNIVERSITY OF ILLINOIS AT CHICAGO
COLLEGE OF MEDICINE
1940 WEST TAYLOR STREET
CHICAGO, IL 60612-7353

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SECTION I
PATHOLOGY NARRATIVE

DRAFT PATHOLOGY REPORT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INTRODUCTION

This pathology report, submitted by Pathology Associates International (PAI) to Toxicology Research Laboratory, University of Illinois at Chicago (UIC/TRL), represents the histopathology findings for the study designated as "Thirteen Week Oral Toxicity Study of WR242511 with a Thirteen Week Recovery Period in Dogs", UIC/TRL Study Number 193.

EXPERIMENTAL DESIGN AND METHODS

Three groups (Groups 2-4), each composed of eight male and eight female Beagle dogs, were given the test article once daily by gelatin capsule starting on Study Day 1 and continuing through Week 13. Animals in Groups 2, 3, and 4 were given 0.1, 0.3, and 1.0 mg of WR242511 Tartrate base/kg body weight/day, respectively. One group (Group 1), composed of eight male and eight female Beagle dogs, was given empty gelatin capsules daily through Week 13. Four animals per sex per group were sacrificed after thirteen weeks and the remaining animals were sacrificed after twenty-six weeks.

All necropsies were performed according to UIC/TRL Standard Operating Procedures and were conducted by PAI personnel. Tissues required by the protocol (see Table II, Protocol-Required Tissues) were examined and placed in 10% neutral buffered formalin, except for eyes, which were placed in 2.5% phosphate buffered glutaraldehyde. Bone marrow smears were prepared from the rib of each animal at necropsy. The bone marrow smears were fixed in methanol, stained with a Wrights-Giemsa stain, and evaluated microscopically to determine the Myeloid:Erythroid (M:E) Ratio.

Tissues required for histopathologic evaluation in all groups were trimmed and processed, and slides were prepared in accordance with PAI Standard Operating Procedures. These tissues, except for tonsil for animal number 8696, for which sublingual salivary gland was inadvertently collected in place of tonsil; cecum, ileum, and colon in animal number 8693, which were found at trimming to be missing from the wet tissues; and mammary gland from animal numbers 8664 and 8681, which was not found in sections because of its small size as a rudimentary tissue in males, were evaluated by light microscopy and the results were tabulated.

Treatment-related lesions are summarized in Table III, Summary of Treatment-Related Lesions. Microscopic findings for all groups are summarized in the Project Summary Tables (Section II). The mean group severity scores are found in the Severity Summary Tables (Section III), which are printed separately for animals removed after 13 weeks and animals removed after 26 weeks. The mean group severity scores for each tissue observation were determined by using weighted averages based on severity and distribution as outlined in Table IV (Severity Weighting Factors). Microscopic findings in the protocol-required tissues for individual animals are presented in the Tabulated Animal Data Tables (Section IV). The correlation of the necropsy findings and histopathology findings are reported in the Correlation of Gross and Microscopic (Micro) Findings (Section V). The codes used as entries in these tables are explained in the Report Codes Table. The bone marrow evaluation results are presented in the Bone Marrow Evaluation Report (Section VII).

RESULTS AND DISCUSSION

The Results and Discussion section is divided into four parts: Necropsy Findings, Diagnostic Terms, Histopathology Findings, and Bone Marrow Evaluation Findings. The Necropsy Findings portion gives lesions seen at necropsy that were test article-related. The Diagnostic Terms portion lists and clarifies

diagnostic terminology that may be unclear. The Histopathology Findings portion of this section reports the results and provides discussion of the histopathologic evaluation of the tissues. The Bone Marrow Evaluation Findings portion of this section reports the results of bone marrow smear evaluations.

Necropsy Findings

Males - Week 14

Multiple white foci were observed in lungs from 0 of 4, 0 of 4, 0 of 4, and 4 of 4 male dogs in Groups 1, 2, 3, and 4, respectively. Wet tissue review of unperfused lung revealed that lungs failed to collapse normally at necropsy in 0 of 4, 0 of 4, 0 of 4, and 3 of 4 male dogs in Groups 1, 2, 3, and 4, respectively. Also, enlarged bronchial lymph nodes were observed in 0 of 4, 0 of 4, 0 of 4, and 2 of 4 male dogs in Groups 1, 2, 3, and 4, respectively.

Males - Week 27

Treatment-related gross lesions were not observed.

Females - Week 14

Multiple white foci were observed in lungs from 0 of 4, 0 of 4, 1 of 4, and 3 of 4 female dogs in Groups 1, 2, 3, and 4, respectively. Wet tissue review of unperfused lung revealed that lungs failed to collapse normally at necropsy in 0 of 4, 0 of 4, 0 of 4, and 2 of 4 female dogs in Groups 1, 2, 3, and 4, respectively. Also, enlarged bronchial lymph nodes were observed in 0 of 4, 0 of 4, 1 of 4, and 3 of 4 female dogs in Groups 1, 2, 3, and 4, respectively.

Females - Week 27

Deformity of left apical lobe was observed in the lung of one Group 3 female (animal number 8701). The deformity was correlated to a focal area of atelectasis. A white focus on the surface of the left apical lobe of lung was observed in one Group 4 female (animal number 8707). The white focus was correlated to a region of chronic interstitial inflammation. Both lesions could be residual effects of lesions similar to those observed in animals sacrificed at 13 weeks.

All other gross lesions are interpreted as incidental findings. All gross lesions present are noted and correlated to histopathology findings when possible in Section V.

Diagnostic Terms

The morphologic characteristics of observations and lesions which require comment are presented in subsequent paragraphs to aid in the interpretation of the data.

Lung

Accumulation of alveolar macrophages was characterized by the presence of numerous macrophages in the lumen of affected alveoli. Macrophages were relatively large with a small nucleus and copious vacuolated cytoplasm. Chronic perivascular inflammation consisted of infiltration of lymphocytes around small vessels, and was generally found in or near collections of alveolar macrophages. Chronic peribronchial inflammation consisted of infiltration of lymphocytes around a single small bronchus. Chronic interstitial inflammation was characterized by the presence of alveolar walls that were thicker than normal because of the presence of fibrous connective tissue, and by the presence of a few lymphocytes and macrophages. Chronic interstitial inflammation was generally associated with more severe cases of alveolar macrophage accumulation. A diagnosis of basophilic granular material denotes the presence of fine basophilic granular material in the lumen of alveoli. Atelectasis consisted of a focal region wherein alveoli were very small with thickened walls.

Bone Marrow (Rib)

Bone marrow hyperplasia was characterized by an increased number of hematopoietic cells and a reduced proportion of large vacuoles that were interpreted as fat cells.

Spleen

Erythropoiesis in spleen was characterized by the presence of colonies of deeply basophilic erythrocyte precursor cells in splenic parenchyma. Background levels of splenic erythropoiesis were higher and more variable in females than in males. The increased variability may be related to reproductive cycle variations. A diagnosis of erythropoiesis was only rendered when the incidence of erythrocyte precursor colonies exceeded that observed in spleen from control females.

The remainder of the diagnoses used in this study were considered to be self-explanatory and were not discussed in this section.

Histopathology Findings

Lung - Week 14

Alveolar macrophage accumulation in lung was observed in 0 of 4 (SEV = 0.00), 0 of 4 (SEV = 0.00), 1 of 4 (SEV = 0.38), and 4 of 4 (SEV = 2.25) male dogs in Groups 1, 2, 3, and 4, respectively. Also, alveolar macrophage accumulation in lung was observed in 2 of 4 (SEV = 0.19), 2 of 4 (SEV = 0.13), 2 of 4 (SEV = 0.75), and 4 of 4 (SEV = 2.25) female dogs in Groups 1, 2, 3, and 4, respectively. The incidence and/or severity of accumulation of alveolar macrophages in lung was increased in Group 3 and 4 dogs (males and females) when compared to Group 1 dogs. Accumulation of alveolar macrophages in lung from the 2 Group 2 female dogs (animal numbers 8703 and 8713) were of such minimal severity that the observations were interpreted as incidental findings. Accumulation of alveolar macrophages was consistent with the presence of some types of foreign material in alveoli of the lung.

The failure of lungs from several high dose animals to deflate normally at necropsy indicates the presence of edema. Histopathologic evidence of edema (acidophilic, homogeneous, or faintly granular material filling alveoli) was not observed in this study, but the fixation and processing methods used would only reveal the presence of relatively acute and severe changes. More sensitive histologic detection of edema would require fixation of unperfused lung in a coagulant fixative. The pathogenesis of lung edema is discussed in some detail by Jubb, et al (Pathology of Domestic Animals, 3rd edition, volume 2, pages 447-450). The recognized "types" of edema are cardiogenic edema, neurogenic edema, and edema caused by damage to alveolar type I epithelium and capillary endothelium. Cardiac and/or neuropathologic lesions consistent with secondary edema were not present in this study. Also, macrophages present in this study were large with foamy cytoplasm, while those characteristic of cardiogenic edema generally contain prominent hemosiderin deposits and some intact erythrocytes. Therefore, the most likely etiology of pulmonary edema in this study would be damage to the alveolar type I epithelium and/or damage to capillary endothelium.

Chronic perivascular inflammation in lung was observed in 0 of 4 (SEV = 0.00), 0 of 4 (SEV = 0.00), 1 of 4 (SEV = 0.38), and 4 of 4 (SEV = 0.50) male dogs in Groups 1, 2, 3, and 4, respectively. Also, chronic perivascular inflammation in lung was observed in 1 of 4 (SEV = 0.06), 2 of 4 (SEV = 0.25), 2 of 4 (SEV = 0.50), and 4 of 4 (SEV = 0.75) female dogs in Groups 1, 2, 3, and 4, respectively. The incidence and severity of chronic perivascular inflammation was increased in Group 4 dogs (male and female) when compared to Group 1 dogs. The perivascular inflammation in Group 3 animals may be related to treatment. However, the minimal chronic perivascular inflammation observed in Group 2 females was not considered to be biologically significant.

Chronic interstitial inflammation in lung was observed in 0 of 4 (SEV = 0.00), 0 of 4 (SEV = 0.00), 1 of 4 (SEV = 0.13), and 3 of 4 (SEV = 0.63) male dogs in Groups 1, 2, 3, and 4, respectively. Also, chronic interstitial inflammation was observed in 1 of 4 (SEV = 0.13), 0 of 4 (SEV = 0.00), 1 of 4 (SEV

= 0.38), and 4 of 4 (SEV = 1.50) female dogs in Groups 1, 2, 3, and 4, respectively. The incidence and severity of chronic interstitial inflammation of lung was increased in Group 4 dogs (male and female) when compared to Group 1 dogs. The interstitial lesion in the Group 3 female (animal number 8706) was of slightly higher severity than the lesion in the control female (animal number 8721), and thus may be related to treatment. Consistent with this observation was the occurrence of this change in 1 of 4 males in Group 3 compared to 0 of 4 Group 1 males.

Chronic interstitial inflammation was generally closely associated with more severe cases of alveolar macrophage accumulation. However, accumulation of alveolar macrophages was not always associated with interstitial changes that were detectable by light microscopy. Therefore, one possible pathogenesis of the changes could be subtle changes to the capillary endothelium and/or alveolar type I epithelium resulting in chronic hemorrhage and edema, which may then cause the alveolar interstitial changes as a secondary response.

Basophilic granular material was found in the lumen of lung alveoli in 0 of 4 (SEV = 0.00), 0 of 4 (SEV = 0.00), 0 of 4 (SEV = 0.00), and 1 of 4 (SEV = 0.63) male dogs in Groups 1, 2, 3, and 4, respectively. Also, basophilic granular material was observed in lung alveoli in 0 of 4 (SEV = 0.00), 0 of 4 (SEV = 0.00), 0 of 4 (SEV = 0.00), and 3 of 4 (SEV = 0.94) female dogs in Groups 1, 2, 3, and 4, respectively. The presence of basophilic granular material in lung alveoli of Group 4 dogs (male and female) was interpreted as a treatment-related finding. Specific staining was not performed, but the basophilic granular material is consistent with bacterial growth, which is a frequently encountered complication of lung edema.

Lung - Week 27

Alveolar macrophage accumulation in lung was observed in 0 of 4 (SEV = 0.00), 0 of 4 (SEV = 0.00), 1 of 4 (SEV = 0.06), and 1 of 4 (SEV = 0.13) male dogs in Groups 1, 2, 3, and 4, respectively. Alveolar macrophage accumulation was not observed in lung from female recovery dogs.

Chronic perivascular inflammation in lung was observed in 0 of 4 (SEV = 0.00), 0 of 4 (SEV = 0.00), 0 of 4 (SEV = 0.00), and 1 of 4 (SEV = 0.13) male dogs in Groups 1, 2, 3, and 4, respectively. Chronic perivascular inflammation was not observed in lung from female recovery dogs.

Chronic interstitial inflammation in lung was observed in 0 of 4 (SEV = 0.00), 0 of 4 (SEV = 0.00), 0 of 4 (SEV = 0.00), and 2 of 4 (SEV = 0.19) male dogs in Groups 1, 2, 3, and 4, respectively. Also, chronic interstitial inflammation in lung was observed in 0 of 4 (SEV = 0.00), 0 of 4 (SEV = 0.00), 1 of 4 (SEV = 0.13), and 2 of 4 (SEV = 0.44) female dogs in Groups 1, 2, 3, and 4, respectively.

Chronic peribronchial inflammation in lung was observed in 0 of 4 (SEV = 0.00), 0 of 4 (SEV = 0.00), 0 of 4 (SEV = 0.00), and 1 of 4 (SEV = 0.06) female dogs in Groups 1, 2, 3, and 4, respectively. Chronic peribronchial inflammation was not observed in lung from male recovery dogs, nor in males and females at Week 14.

Lung lesions observed in recovery animals were generally of minimal severity and always affected a very limited area of lung parenchyma. Therefore, although treatment-related lesions were not completely resolved after 13 weeks of recovery, lesions were resolved to a point where they were considered to be biologically insignificant.

Lymph Node, Bronchial - Week 14

Bronchial lymph nodes were collected as gross lesions from some Group 3 and Group 4 animals. In all cases, enlargement of bronchial lymph nodes observed at necropsy was due to accumulation of macrophages in the lymph node sinuses. Enlarged bronchial lymph nodes were not observed in recovery animals.

Bone Marrow (Rib) - Week 14

Bone marrow hyperplasia in rib was observed in 0 of 4 (SEV = 0.00), 1 of 4 (SEV = 0.25), 4 of 4 (SEV = 1.75), and 4 of 4 (SEV = 2.75) male dogs in Groups 1, 2, 3, and 4, respectively. Also, bone marrow hyperplasia in rib was observed in 0 of 4 (SEV = 0.00), 0 of 4 (SEV = 0.00), 2 of 4 (SEV = 0.50), and 4 of 4 (SEV = 1.50) female dogs in Groups 1, 2, 3, and 4, respectively. The incidence and/or severity of bone marrow hyperplasia in Groups 3 and 4 (male and female) was considered to be increased relative to Group 1, but bone marrow hyperplasia in Group 2 (male and female) dogs was not significantly affected by test article treatment.

Bone Marrow (Rib) - Week 27

There were no treatment-related lesions in rib after 13 weeks of treatment followed by 13 weeks of recovery.

Spleen - Week 14

Erythropoiesis in spleen was observed in 0 of 4 (SEV = 0.00), 0 of 4 (SEV = 0.00), 2 of 4 (SEV = 0.50), and 2 of 4 (SEV = 0.75) female dogs in Groups 1, 2, 3, and 4, respectively. The erythropoiesis in spleen from Group 3 and 4 female dogs was considered to be related to treatment. Erythropoiesis was not observed in spleen from male dogs.

Spleen - Week 27

There were no treatment-related lesions in spleen after 13 weeks of treatment followed by 13 weeks of recovery.

All other lesions observed in this study were interpreted as incidental findings.

Bone Marrow Evaluation Findings (Section VII)

The evaluation of bone marrow smears collected during Week 14 in this study indicated a decrease in the M:E Ratios in male and female dogs receiving 1.0 mg base/kg/day. The decrease was statistically significant in the female dogs. For this reason, bone marrow was also evaluated from the recovery animals. The M:E Ratios from bone marrow smears collected from these animals were all considered to be within normal limits.

CONCLUSIONS

Under the conditions of this study, daily administration of WR242511 Tartrate in gelatin capsules at a dosage of 0.3 or 1.0 mg base/kg body weight to dogs for 13 weeks resulted in lung lesions (alveolar macrophage accumulation, chronic perivascular inflammation, chronic interstitial inflammation, and basophilic granular material), bronchial lymph node lesions (macrophage accumulation), bone marrow hyperplasia in rib, and increased erythropoiesis in spleen. Also, daily administration of WR242511 Tartrate in gelatin capsules at a dosage of 1.0 mg base/kg body weight to dogs for 13 weeks resulted in a decreased M:E Ratio of the rib bone marrow, indicating that the bone marrow hyperplasia was primarily erythroid in nature. Similar administration of WR242511 Tartrate at a dosage of 0.1 mg base/kg body weight did not result in clinically significant treatment-related effects. The lung lesions seen in Week 14 had essentially resolved by the end of the 13 week recovery period. The residual effects in Groups 3 and 4 after the 13 week recovery period were of such minimal severity that they were not considered to be clinically significant. Treatment-related effects observed at Week 14 in spleen, bone marrow, and bronchial lymph nodes had also resolved by the end of the 13 week recovery period.

Robert L. Morrissey, DVM, Ph.D.
Diplomate, ACVP

Date

TABLE I

SUMMARY OF EXPERIMENTAL DESIGN

Treatment Group	Dose Level (mg base/kg/day)	Number of Males		Number of Females	
		Week 14	Week 27*	Week 14	Week 27*
1	0	4	4	4	4
2	0.1	4	4	4	4
3	0.3	4	4	4	4
4	1.0	4	4	4	4

* Recovery Animals

TABLE II
PROTOCOL-REQUIRED TISSUES -

Adrenal glands	Parathyroid glands
Aorta (thoracic)	Pituitary gland
Bone marrow (from rib)	Prostate
Brain (fore-, mid-, and hind-)	Rib
Cecum	Salivary gland (mandibular)
Colon	Sciatic nerve
Diaphragm	Skeletal muscle
Duodenum	Skin
Esophagus	Spinal cord (cervical)
Eyes (including optic nerve)	Spinal cord (thoracic)
Gallbladder	Spleen
Heart	Stomach
Ileum	Testes
Jejunum	Thymus
Kidneys	Thyroid gland
Liver	Tongue
Lungs	Tonsil
Lymph node (mesenteric)	Trachea
Lymph node (mandibular)	Ureter
Mammary gland	Urinary bladder
Ovaries	Uterus
Pancreas	Gross lesions

TABLE III
SUMMARY OF TREATMENT-RELATED LESIONS

		Week 14				Week 27			
		Dose (mg base/kg/day)							
		0	0.1	0.3	1.0	0	0.1	0.3	1.0
ORGAN - lesion	Sex								
LUNG									
- Accumulation, alveolar macrophage	M	0/4 (0.00)*	0/4 (0.00)	1/4 (0.38)	4/4 (2.25)	0/4 (0.00)	0/4 (0.00)	1/4 (0.06)	1/4 (0.13)
	F	2/4 (0.19)	2/4 (0.13)	2/4 (0.75)	4/4 (2.25)	0/4 (0.00)	0/4 (0.00)	0/4 (0.00)	0/4 (0.00)
- Inflammation chronic, perivascular	M	0/4 (0.00)	0/4 (0.00)	1/4 (0.38)	4/4 (0.50)	0/4 (0.00)	0/4 (0.00)	0/4 (0.00)	1/4 (0.13)
	F	1/4 (0.06)	2/4 (0.25)	2/4 (0.50)	4/4 (0.75)	0/4 (0.00)	0/4 (0.00)	0/4 (0.00)	0/4 (0.00)
- Inflammation chronic, interstitium	M	0/4 (0.00)	0/4 (0.00)	1/4 (0.13)	3/4 (0.63)	0/4 (0.00)	0/4 (0.00)	0/4 (0.00)	2/4 (0.19)
	F	1/4 (0.13)	0/4 (0.00)	1/4 (0.38)	4/4 (1.50)	0/4 (0.00)	0/4 (0.00)	1/4 (0.13)	2/4 (0.44)
- Basophilic granular material	M	0/4 (0.00)	0/4 (0.00)	0/4 (0.00)	1/4 (0.63)	0/4 (0.00)	0/4 (0.00)	0/4 (0.00)	0/4 (0.00)
	F	0/4 (0.00)	0/4 (0.00)	0/4 (0.00)	3/4 (0.94)	0/4 (0.00)	0/4 (0.00)	0/4 (0.00)	0/4 (0.00)
- Inflammation chronic, peribronchial	M	0/4 (0.00)	0/4 (0.00)	0/4 (0.00)	0/4 (0.00)	0/4 (0.00)	0/4 (0.00)	0/4 (0.00)	0/4 (0.00)
	F	0/4 (0.00)	0/4 (0.00)	0/4 (0.00)	0/4 (0.00)	0/4 (0.00)	0/4 (0.00)	0/4 (0.00)	1/4 (0.06)
LYMPH NODE, BRONCHIAL									
- Accumulation, macrophage	M	-	-	-	2/2 (3.00)	-	-	-	-
	F	-	-	1/1 (2.00)	3/3 (3.00)	-	-	-	-
BONE MARROW (RIB)									
- Hyperplasia	M	0/4 (0.00)	1/4 (0.25)	4/4 (1.75)	4/4 (2.75)	0/4 (0.00)	0/4 (0.00)	0/4 (0.00)	0/4 (0.00)
	F	0/4 (0.00)	0/4 (0.00)	2/4 (0.50)	4/4 (1.50)	0/4 (0.00)	0/4 (0.00)	0/4 (0.00)	0/4 (0.00)
SPLEEN									
- Erythropoiesis	M	0/4 (0.00)	0/4 (0.00)	0/4 (0.00)	0/4 (0.00)	0/4 (0.00)	0/4 (0.00)	0/4 (0.00)	0/4 (0.00)
	F	0/4 (0.00)	0/4 (0.00)	2/4 (0.50)	2/4 (0.75)	0/4 (0.00)	0/4 (0.00)	0/4 (0.00)	0/4 (0.00)

* Incidence (mean group severity score)

- None examined

Lesion severity as modified by distribution is defined in Table IV.

TABLE IV

SEVERITY WEIGHTING FACTORS

The PAI pathology computer system (LABCAT®) has a built-in weighting system for calculating the average severity for each tissue observation. These weighted averages are based upon the severity and distribution as outlined in the following table.

Severity Grading	No Modifier	Focal	Multifocal	Diffuse
1	1.0	0.25	0.5	0.75
2	2.0	1.25	1.5	1.75
3	3.0	2.25	2.5	2.75
4	4.0	3.25	3.5	3.75

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 193

Report Codes Table

A. Codes applying to organs

N	Tissues within normal histological limits
A	Autolysis precluding adequate evaluation
U	Tissues unavailable/unsuitable for complete evaluation
*	Tissues not required by protocol

B. Codes applying to microscopic diagnoses

1	minimal
2	mild
3	moderate
4	marked
()	focal
[]	diffuse
< >	multifocal
P	Present
B	Neoplasm, benign
M	Neoplasm, malignant without metastasis
C	Neoplasm, malignant with metastasis
X	Metastatic site (+)
I	Bilateral
L	Unilateral
-	No data entered

SECTION II
PROJECT SUMMARY TABLE

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

PROJECT SUMMARY

STUDY ID : TRL SM 193

STUDY NUMBER: 193

FATE: ALL

DAYS ON TEST: ALL

SEX: MALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	8	8	8	8
	# %	# %	# %	# %
BRAIN (FORE)	# EX 4	4	4	4
SPINAL CORD (CERVICAL)	# EX 4	4	4	4
Inflammation, chronic	1 25.0	0 0.0	0 0.0	0 0.0
BRAIN (MID)	# EX 4	4	4	4
BRAIN (HIND)	# EX 4	4	4	4
SPINAL CORD (THORACIC)	# EX 4	4	4	4
HEART	# EX 4	4	4	4
AORTA	# EX 4	4	4	4
TRACHEA	# EX 4	4	4	4
Inflammation, chronic	2 50.0	1 25.0	3 75.0	1 25.0
ESOPHAGUS	# EX 4	4	4	4
LUNG	# EX 8	8	8	8
Accumulation, alveolar macrophage	0 0.0	0 0.0	2 25.0	5 63.0
Inflammation, chronic, perivascular	0 0.0	0 0.0	1 13.0	5 63.0
Inflammation, chronic, interstitium	0 0.0	0 0.0	1 13.0	5 63.0
Basophilic granular material	0 0.0	0 0.0	0 0.0	1 13.0
KIDNEY, RIGHT	# EX 4	4	4	4
Mineralization, medulla	4 100.0	4 100.0	4 100.0	4 100.0
Infarction	1 25.0	0 0.0	1 25.0	0 0.0
Mineralization, cortex	1 25.0	0 0.0	1 25.0	0 0.0
Eosinophilic casts	0 0.0	0 0.0	1 25.0	0 0.0

Incidence Calculated by No. of Tissues Scored

(3) - 0.3 mg base/kg/day

(1) - 0 mg base/kg/day

(4) - 1.0 mg base/kg/day

(2) - 0.1 mg base/kg/day

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

PROJECT SUMMARY

STUDY ID : TRL SN 193

STUDY NUMBER: 193

FATE: ALL

DAYS ON TEST: ALL

SEX: MALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	8	8	8	8
KIDNEY, LEFT	# EX 4	4	4	4
Mineralization, medulla	3 75.0	3 75.0	4 100.0	3 75.0
Inflammation, chronic	1 25.0	0 0.0	0 0.0	0 0.0
Eosinophilic casts	0 0.0	0 0.0	1 25.0	0 0.0
Infarction	0 0.0	0 0.0	1 25.0	0 0.0
SPLEEN	# EX 8	8	8	8
Siderotic nodule	1 13.0	0 0.0	0 0.0	0 0.0
PANCREAS	# EX 4	4	4	4
DUODENUM	# EX 4	4	4	4
LIVER	# EX 4	4	4	4
Inflammation, chronic	3 75.0	4 100.0	4 100.0	4 100.0
Extramedullary hematopoiesis	2 50.0	3 75.0	3 75.0	3 75.0
GALLBLADDER	# EX 4	4	4	4
Hyperplasia, lymphoid	3 75.0	1 25.0	2 50.0	4 100.0
ADRENAL GLAND	# EX 4	4	4	4
SALIVARY GLAND	# EX 4	4	4	4
Inflammation, chronic	0 0.0	1 25.0	1 25.0	1 25.0
LYMPH NODE, MANDIBULAR	# EX 4	4	4	4
Hemorrhage	1 25.0	0 0.0	0 0.0	0 0.0
Pigmentation, macrophage	2 50.0	1 25.0	0 0.0	1 25.0
JEJUNUM	# EX 4	4	4	4

Incidence Calculated by No. of Tissues Scored

(1) - 0 mg base/kg/day

(2) - 0.1 mg base/kg/day

(3) - 0.3 mg base/kg/day

(4) - 1.0 mg base/kg/day

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

PROJECT SUMMARY

STUDY ID : TRL SN 193

STUDY NUMBER: 193

FATE: ALL

DAYS ON TEST: ALL

SEX: MALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	8	8	8	8
	# %	# %	# %	# %
COLON	# EX 4	4	4	4
TONSIL	# EX 4	4	4	4
ILEUM	# EX 4	4	4	4
LYMPH NODE, MESENTERIC	# EX 4	4	4	4
Hemorrhage	4 100.0	2 50.0	2 50.0	4 100.0
TONGUE	# EX 4	4	4	4
DIAPHRAGM	# EX 4	4	4	4
THYMUS	# EX 4	4	4	4
PROSTATE	# EX 4	4	4	4
SKELETAL MUSCLE	# EX 4	4	4	4
SKIN	# EX 4	4	4	4
MAMMARY GLAND	# EX 4	4	4	2
THYROID GLAND	# EX 4	4	4	4
PARATHYROID GLAND	# EX 4	4	4	4
PITUITARY GLAND	# EX 4	4	4	4
Cyst	1 25.0	3 75.0	2 50.0	2 50.0

Incidence Calculated by No. of Tissues Scored

(1) - 0 mg base/kg/day

(2) - 0.1 mg base/kg/day

(3) - 0.3 mg base/kg/day

(4) - 1.0 mg base/kg/day

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

PROJECT SUMMARY

STUDY ID : TRL SN 193

STUDY NUMBER: 193

FATE: ALL

DAYS ON TEST: ALL

SEX: MALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	8	8	8	8
	# %	# %	# %	# %
CECUM	# EX 4	4	4	4
Cyst, crypt	0 0.0	0 0.0	0 0.0	1 25.0
STOMACH	# EX 4	4	4	4
Hyperplasia, lymphoid, submucosa	3 75.0	4 100.0	3 75.0	3 75.0
URINARY BLADDER	# EX 4	4	4	4
TESTES	# EX 4	4	4	4
SCIATIC NERVE	# EX 4	4	4	4
URETER	# EX 4	4	4	4
EYE	# EX 4	4	4	4
OPTIC NERVE	# EX 4	4	4	4
BONE MARROW (RIB)	# EX 8	8	8	8
Hyperplasia	0 0.0	1 13.0	4 50.0	4 50.0
BONE (RIB)	# EX 4	4	4	4
LYMPH NODE, BRONCHIAL	# EX 0	0	0	2
Accumulation, macrophage	0 0.0	0 0.0	0 0.0	2 100.0

Incidence Calculated by No. of Tissues Scored

(3) - 0.3 mg base/kg/day

(1) - 0 mg base/kg/day

(4) - 1.0 mg base/kg/day

(2) - 0.1 mg base/kg/day

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

PROJECT SUMMARY

STUDY ID : TRL SN 193

STUDY NUMBER: 193

FATE: ALL

DAYS ON TEST: ALL

SEX: FEMALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	8	8	8	8
	#	%	#	%
BRAIN (FORE)	# EX 4		4	
SPINAL CORD (CERVICAL)	# EX 4		4	
BRAIN (MID)	# EX 4		4	
Inflammation, chronic	0 0.0	0 0.0	0 0.0	1 25.0
BRAIN (HIND)	# EX 4		4	
SPINAL CORD (THORACIC)	# EX 4		4	
HEART	# EX 4		4	
Degeneration, mucoid, valve	0 0.0	1 25.0	1 25.0	0 0.0
AORTA	# EX 4		4	
TRACHEA	# EX 4		4	
Inflammation, chronic	0 0.0	2 50.0	1 25.0	0 0.0
ESOPHAGUS	# EX 4		4	
Inflammation, chronic	1 25.0	0 0.0	0 0.0	0 0.0
LUNG	# EX 8		8	
Accumulation, alveolar macrophage	2 25.0	2 25.0	2 25.0	4 50.0
Inflammation, chronic, perivascular	1 13.0	2 25.0	2 25.0	4 50.0
Inflammation, chronic, interstitium	1 13.0	0 0.0	2 25.0	6 75.0
Basophilic granular material	0 0.0	0 0.0	0 0.0	3 38.0
Atelectasis	0 0.0	0 0.0	1 13.0	0 0.0
Inflammation, chronic, peribronchial	0 0.0	0 0.0	0 0.0	1 13.0

Incidence Calculated by No. of Tissues Scored

(1) - 0 mg base/kg/day

(2) - 0.1 mg base/kg/day

(3) - 0.3 mg base/kg/day

(4) - 1.0 mg base/kg/day

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

PROJECT SUMMARY

STUDY ID : TRL SN 193

STUDY NUMBER: 193

FATE: ALL

DAYS ON TEST: ALL

SEX: FEMALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	8	8	8	8
	# %	# %	# %	# %
KIDNEY, RIGHT	# EX 4	4	4	4
Mineralization, medulla	3 75.0	4 100.0	4 100.0	3 75.0
Inflammation, chronic	0 0.0	1 25.0	0 0.0	0 0.0
KIDNEY, LEFT	# EX 4	4	4	4
Mineralization, medulla	3 75.0	4 100.0	3 75.0	4 100.0
Eosinophilic casts	0 0.0	0 0.0	1 25.0	0 0.0
Infarction	0 0.0	0 0.0	1 25.0	0 0.0
Mineralization, cortex	1 25.0	0 0.0	0 0.0	0 0.0
SPLEEN	# EX 8	8	8	8
Erythropoiesis	0 0.0	0 0.0	2 25.0	2 25.0
PANCREAS	# EX 4	4	4	4
DUODENUM	# EX 4	4	4	4
LIVER	# EX 4	4	4	4
Inflammation, chronic	3 75.0	4 100.0	4 100.0	2 50.0
Extramedullary hematopoiesis	4 100.0	2 50.0	4 100.0	4 100.0
GALLBLADDER	# EX 4	4	4	4
Hyperplasia, lymphoid	3 75.0	3 75.0	2 50.0	3 75.0
ADRENAL GLAND	# EX 4	4	4	4
SALIVARY GLAND	# EX 4	4	4	4
LYMPH NODE, MANDIBULAR	# EX 4	4	4	4
Hemorrhage	1 25.0	0 0.0	0 0.0	1 25.0
Pigmentation, macrophage	0 0.0	1 25.0	2 50.0	1 25.0

Incidence Calculated by No. of Tissues Scored

(3) - 0.3 mg base/kg/day

(1) - 0 mg base/kg/day

(4) - 1.0 mg base/kg/day

(2) - 0.1 mg base/kg/day

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PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

PROJECT SUMMARY

STUDY ID : TRL SN 193

STUDY NUMBER: 193

FATE: ALL

DAYS ON TEST: ALL

SEX: FEMALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	8	8	8	8
	# %	# %	# %	# %
JEJUNUM	# EX 4	4	4	4
COLON	# EX 4	3	4	4
TONSIL	# EX 4	4	4	3
Bacterial colony	0 0.0	1 25.0	0 0.0	1 33.0
ILEUM	# EX 4	3	4	4
LYMPH NODE, MESENTERIC	# EX 4	4	4	4
Hemorrhage	2 50.0	2 50.0	4 100.0	2 50.0
TONGUE	# EX 4	4	4	4
DIAPHRAGM	# EX 4	4	4	4
THYMUS	# EX 4	4	4	4
SKELETAL MUSCLE	# EX 4	4	4	4
SKIN	# EX 4	4	4	4
MAMMARY GLAND	# EX 4	4	4	4
Lactation	1 25.0	0 0.0	2 50.0	1 25.0
THYROID GLAND	# EX 4	4	4	4
Cyst	2 50.0	0 0.0	0 0.0	0 0.0
PARATHYROID GLAND	# EX 4	4	4	4
Cyst	0 0.0	0 0.0	0 0.0	1 25.0

Incidence Calculated by No. of Tissues Scored

(3) - 0.3 mg base/kg/day

(1) - 0 mg base/kg/day

(4) - 1.0 mg base/kg/day

(2) - 0.1 mg base/kg/day

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

PROJECT SUMMARY

STUDY ID : TRL SN 193

STUDY NUMBER: 193

FATE: ALL

DAYS ON TEST: ALL

SEX: FEMALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	8	8	8	8
	# %	# %	# %	# %
PITUITARY GLAND	# EX 4	4	4	4
Cyst	3 75.0	2 50.0	1 25.0	2 50.0
CECUM	# EX 4	3	4	4
Cyst, crypt	0 0.0	0 0.0	1 25.0	0 0.0
STOMACH	# EX 4	4	4	4
Hyperplasia, lymphoid, submucosa	4 100.0	4 100.0	3 75.0	4 100.0
URINARY BLADDER	# EX 4	4	4	4
OVARY	# EX 4	4	4	4
Cyst	1 25.0	1 25.0	0 0.0	0 0.0
Corpora lutea	1 25.0	2 50.0	3 75.0	1 25.0
UTERUS	# EX 4	4	4	4
SCIATIC NERVE	# EX 4	4	4	4
URETER	# EX 4	4	4	4
EYE	# EX 4	4	4	4
OPTIC NERVE	# EX 4	4	4	4
BONE MARROW (RIB)	# EX 8	8	8	8
Hyperplasia	0 0.0	0 0.0	2 25.0	4 50.0
BONE (RIB)	# EX 4	4	4	4

Incidence Calculated by No. of Tissues Scored

(1) - 0 mg base/kg/day

(2) - 0.1 mg base/kg/day

(3) - 0.3 mg base/kg/day

(4) - 1.0 mg base/kg/day

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

PROJECT SUMMARY

STUDY ID : TRL SM 193

STUDY NUMBER: 193

FATE: ALL

DAYS ON TEST: ALL

SEX: FEMALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	8	8	8	8

	#	%	#	%	#	%	#	%	
LYMPH NODE, BRONCHIAL	# EX	0		0		1		3	
Accumulation, macrophage		0	0.0	0	0.0	1	100.0	3	100.0

Incidence Calculated by No. of Tissues Scored

(1) - 0 mg base/kg/day

(2) - 0.1 mg base/kg/day

(3) - 0.3 mg base/kg/day

(4) - 1.0 mg base/kg/day

SECTION III
SEVERITY SUMMARY TABLE

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

SEVERITY SUMMARY

STUDY ID : TRL SN 193

STUDY NUMBER: 193

FATE: ALL

DAYS ON TEST: 92-92

SEX: MALE

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	4	4	4	4
	# SEV	# SEV	# SEV	# SEV
BRAIN (FORE)	# EX 4	4	4	4
SPINAL CORD (CERVICAL)	# EX 4	4	4	4
Inflammation, chronic	1 0.06	0 0.00	0 0.00	0 0.00
BRAIN (MID)	# EX 4	4	4	4
BRAIN (HIND)	# EX 4	4	4	4
SPINAL CORD (THORACIC)	# EX 4	4	4	4
HEART	# EX 4	4	4	4
AORTA	# EX 4	4	4	4
TRACHEA	# EX 4	4	4	4
Inflammation, chronic	2 0.13	1 0.13	3 0.19	1 0.06
ESOPHAGUS	# EX 4	4	4	4
LUNG	# EX 4	4	4	4
Accumulation, alveolar macrophage	0 0.00	0 0.00	1 0.38	4 2.25
Inflammation, chronic, perivascular	0 0.00	0 0.00	1 0.38	4 0.50
Inflammation, chronic, interstitium	0 0.00	0 0.00	1 0.13	3 0.63
Basophilic granular material	0 0.00	0 0.00	0 0.00	1 0.63
KIDNEY, RIGHT	# EX 4	4	4	4
Mineralization, medulla	4 0.75	4 0.75	4 0.75	4 0.50
Infarction	1 0.31	0 0.00	1 0.38	0 0.00
Mineralization, cortex	1 0.31	0 0.00	1 0.38	0 0.00
Eosinophilic casts	0 0.00	0 0.00	1 0.06	0 0.00

Severity Calculated by No. of Tissues Scored

(3) - 0.3 mg base/kg/day

(1) - 0 mg base/kg/day

(4) - 1.0 mg base/kg/day

(2) - 0.1 mg base/kg/day

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

SEVERITY SUMMARY

STUDY ID : TRL SN 193

STUDY NUMBER: 193

FATE: ALL

DAYS ON TEST: 92-92

SEX: MALE

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	4	4	4	4
	# SEV	# SEV	# SEV	# SEV
KIDNEY, LEFT	# EX 4	4	4	4
Mineralization, medulla	3 0.38	3 0.38	4 0.50	3 0.63
Inflammation, chronic	1 0.13	0 0.00	0 0.00	0 0.00
Eosinophilic casts	0 0.00	0 0.00	1 0.13	0 0.00
Infarction	0 0.00	0 0.00	1 0.56	0 0.00
SPLEEN	# EX 4	4	4	4
Siderotic nodule	1 0.31	0 0.00	0 0.00	0 0.00
PANCREAS	# EX 4	4	4	4
DUODENUM	# EX 4	4	4	4
LIVER	# EX 4	4	4	4
Inflammation, chronic	3 0.38	4 0.50	4 0.50	4 0.50
Extramedullary hematopoiesis	2 0.25	3 0.63	3 0.63	3 0.38
GALLBLADDER	# EX 4	4	4	4
Hyperplasia, lymphoid	3 0.31	1 0.06	2 0.25	4 0.38
ADRENAL GLAND	# EX 4	4	4	4
SALIVARY GLAND	# EX 4	4	4	4
Inflammation, chronic	0 0.00	1 0.31	1 0.06	1 0.06
LYMPH NODE, MANDIBULAR	# EX 4	4	4	4
Hemorrhage	1 0.25	0 0.00	0 0.00	0 0.00
Pigmentation, macrophage	2 0.19	1 0.06	0 0.00	1 0.38
JEJUNUM	# EX 4	4	4	4

Severity Calculated by No. of Tissues Scored

(3) - 0.3 mg base/kg/day

(1) - 0 mg base/kg/day

(4) - 1.0 mg base/kg/day

(2) - 0.1 mg base/kg/day

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

SEVERITY SUMMARY

STUDY ID : TRL SN 193

STUDY NUMBER: 193

FATE: ALL

DAYS ON TEST: 92-92

SEX: MALE

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	4	4	4	4
	# SEV	# SEV	# SEV	# SEV
COLON	# EX 4	4	4	4
TONSIL	# EX 4	4	4	4
ILEUM	# EX 4	4	4	4
LYMPH NODE, MESENTERIC	# EX 4	4	4	4
Hemorrhage	4 0.88	2 0.75	2 1.00	4 1.00
TONGUE	# EX 4	4	4	4
DIAPHRAGM	# EX 4	4	4	4
THYMUS	# EX 4	4	4	4
PROSTATE	# EX 4	4	4	4
SKELETAL MUSCLE	# EX 4	4	4	4
SKIN	# EX 4	4	4	4
MAMMARY GLAND	# EX 4	4	4	2
THYROID GLAND	# EX 4	4	4	4
PARATHYROID GLAND	# EX 4	4	4	4
PITUITARY GLAND	# EX 4	4	4	4
Cyst	1 0.13	3 0.38	2 0.19	2 0.25
CECUM	# EX 4	4	4	4
Cyst, crypt	0 0.00	0 0.00	0 0.00	1 0.06

Severity Calculated by No. of Tissues Scored

(3) - 0.3 mg base/kg/day

(1) - 0 mg base/kg/day

(4) - 1.0 mg base/kg/day

(2) - 0.1 mg base/kg/day

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

SEVERITY SUMMARY

STUDY ID : TRL SN 193

STUDY NUMBER: 193

FATE: ALL

DAYS ON TEST: 92-92

SEX: MALE

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	4	4	4	4
	# SEV	# SEV	# SEV	# SEV
STOMACH	# EX 4	4	4	4
Hyperplasia, lymphoid, submucosa	3 0.31	4 0.44	3 0.63	3 0.38
URINARY BLADDER	# EX 4	4	4	4
TESTES	# EX 4	4	4	4
SCIATIC NERVE	# EX 4	4	4	4
URETER	# EX 4	4	4	4
EYE	# EX 4	4	4	4
OPTIC NERVE	# EX 4	4	4	4
BONE MARROW (RIB)	# EX 4	4	4	4
Hyperplasia	0 0.00	1 0.25	4 1.75	4 2.75
BONE (RIB)	# EX 4	4	4	4
LYMPH NODE, BRONCHIAL	# EX 0	0	0	2
Accumulation, macrophage	0 0.00	0 0.00	0 0.00	2 3.00

Severity Calculated by No. of Tissues Scored

(1) - 0 mg base/kg/day

(2) - 0.1 mg base/kg/day

(3) - 0.3 mg base/kg/day

(4) - 1.0 mg base/kg/day

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

SEVERITY SUMMARY

STUDY ID : TRL SN 193

STUDY NUMBER: 193

FATE: ALL

DAYS ON TEST: 183-183

SEX: MALE

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	4	4	4	4
	# SEV	# SEV	# SEV	# SEV
LUNG	# EX 4	4	4	4
Accumulation, alveolar macrophage	0 0.00	0 0.00	1 0.06	1 0.13
Inflammation, chronic, perivascular	0 0.00	0 0.00	0 0.00	1 0.13
Inflammation, chronic, interstitium	0 0.00	0 0.00	0 0.00	2 0.19
SPLEEN	# EX 4	4	4	4
BONE MARROW (RIB)	# EX 4	4	4	4

Severity Calculated by No. of Tissues Scored

(1) - 0 mg base/kg/day

(2) - 0.1 mg base/kg/day

(3) - 0.3 mg base/kg/day

(4) - 1.0 mg base/kg/day

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

SEVERITY SUMMARY

STUDY ID : TRL SN 193

STUDY NUMBER: 193

FATE: ALL

DAYS ON TEST: 93-93

SEX: FEMALE

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	4	4	4	4
	# SEV	# SEV	# SEV	# SEV
BRAIN (FORE)	# EX 4	4	4	4
SPINAL CORD (CERVICAL)	# EX 4	4	4	4
BRAIN (MID)	# EX 4	4	4	4
Inflammation, chronic	0 0.00	0 0.00	0 0.00	1 0.06
BRAIN (HIND)	# EX 4	4	4	4
SPINAL CORD (THORACIC)	# EX 4	4	4	4
HEART	# EX 4	4	4	4
Degeneration, mucoid, valve	0 0.00	1 0.44	1 0.44	0 0.00
AORTA	# EX 4	4	4	4
TRACHEA	# EX 4	4	4	4
Inflammation, chronic	0 0.00	2 0.13	1 0.13	0 0.00
ESOPHAGUS	# EX 4	4	4	4
Inflammation, chronic	1 0.06	0 0.00	0 0.00	0 0.00
LUNG	# EX 4	4	4	4
Accumulation, alveolar macrophage	2 0.19	2 0.13	2 0.75	4 2.25
Inflammation, chronic, perivascular	1 0.06	2 0.25	2 0.50	4 0.75
Inflammation, chronic, interstitium	1 0.13	0 0.00	1 0.38	4 1.50
Basophilic granular material	0 0.00	0 0.00	0 0.00	3 0.94
KIDNEY, RIGHT	# EX 4	4	4	4
Mineralization, medulla	3 0.38	4 0.50	4 0.75	3 0.38
Inflammation, chronic	0 0.00	1 0.06	0 0.00	0 0.00

Severity Calculated by No. of Tissues Scored

(1) - 0 mg base/kg/day

(2) - 0.1 mg base/kg/day

(3) - 0.3 mg base/kg/day

(4) - 1.0 mg base/kg/day

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

SEVERITY SUMMARY

STUDY ID : TRL SN 193

STUDY NUMBER: 193

FATE: ALL

DAYS ON TEST: 93-93

SEX: FEMALE

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	4	4	4	4
	# SEV	# SEV	# SEV	# SEV
KIDNEY, LEFT	# EX 4	4	4	4
Mineralization, medulla	3 0.38	4 0.50	3 0.63	4 0.50
Eosinophilic casts	0 0.00	0 0.00	1 0.31	0 0.00
Infarction	0 0.00	0 0.00	1 0.31	0 0.00
Mineralization, cortex	1 0.06	0 0.00	0 0.00	0 0.00
SPLEEN	# EX 4	4	4	4
Erythropoiesis	0 0.00	0 0.00	2 0.50	2 0.75
PANCREAS	# EX 4	4	4	4
DUODENUM	# EX 4	4	4	4
LIVER	# EX 4	4	4	4
Inflammation, chronic	3 0.38	4 0.50	4 0.50	2 0.25
Extramedullary hematopoiesis	4 0.50	2 0.25	4 0.50	4 1.00
GALLBLADDER	# EX 4	4	4	4
Hyperplasia, lymphoid	3 0.31	3 0.31	2 0.44	3 0.25
ADRENAL GLAND	# EX 4	4	4	4
SALIVARY GLAND	# EX 4	4	4	4
LYMPH NODE, MANDIBULAR	# EX 4	4	4	4
Hemorrhage	1 0.25	0 0.00	0 0.00	1 0.25
Pigmentation, macrophage	0 0.00	1 0.13	2 0.19	1 0.13
JEJUNUM	# EX 4	4	4	4
COLON	# EX 4	3	4	4

Severity Calculated by No. of Tissues Scored

(3) - 0.3 mg base/kg/day

(1) - 0 mg base/kg/day

(4) - 1.0 mg base/kg/day

(2) - 0.1 mg base/kg/day

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

SEVERITY SUMMARY

STUDY ID : TRL SN 193

STUDY NUMBER: 193

FATE: ALL

DAYS ON TEST: 93-93

SEX: FEMALE

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	4	4	4	4
	# SEV	# SEV	# SEV	# SEV
TONSIL	# EX 4	4	4	3
Bacterial colony	0 0.00	1 0.31	0 0.00	1 1.08
ILEUM	# EX 4	3	4	4
LYMPH NODE, MESENTERIC	# EX 4	4	4	4
Hemorrhage	2 0.75	2 0.75	4 1.00	2 0.50
TONGUE	# EX 4	4	4	4
DIAPHRAGM	# EX 4	4	4	4
THYMUS	# EX 4	4	4	4
SKELETAL MUSCLE	# EX 4	4	4	4
SKIN	# EX 4	4	4	4
MAMMARY GLAND	# EX 4	4	4	4
THYROID GLAND	# EX 4	4	4	4
Cyst	2 0.38	0 0.00	0 0.00	0 0.00
PARATHYROID GLAND	# EX 4	4	4	4
Cyst	0 0.00	0 0.00	0 0.00	1 0.31
PITUITARY GLAND	# EX 4	4	4	4
Cyst	3 1.06	2 0.50	1 0.31	2 0.69
CECUM	# EX 4	3	4	4
Cyst, crypt	0 0.00	0 0.00	1 0.06	0 0.00

Severity Calculated by No. of Tissues Scored

(1) - 0 mg base/kg/day

(2) - 0.1 mg base/kg/day

(3) - 0.3 mg base/kg/day

(4) - 1.0 mg base/kg/day

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

SEVERITY SUMMARY

STUDY ID : TRL SN 193		STUDY NUMBER: 193			
FATE: ALL					
DAYS ON TEST: 93-93		SEX: FEMALE			
GROUP:		1	2	3	4
		(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:		4	4	4	4
	# SEV	# SEV	# SEV	# SEV	
STOMACH	# EX 4	4	4	4	
Hyperplasia, lymphoid, submucosa	4 1.00	4 0.50	3 0.63	4 0.75	
URINARY BLADDER	# EX 4	4	4	4	
OVARY	# EX 4	4	4	4	
Cyst	1 0.31	1 0.31	0 0.00	0 0.00	
UTERUS	# EX 4	4	4	4	
SCIATIC NERVE	# EX 4	4	4	4	
URETER	# EX 4	4	4	4	
EYE	# EX 4	4	4	4	
OPTIC NERVE	# EX 4	4	4	4	
BONE MARROW (RIB)	# EX 4	4	4	4	
Hyperplasia	0 0.00	0 0.00	2 0.50	4 1.50	
BONE (RIB)	# EX 4	4	4	4	
LYMPH NODE, BRONCHIAL	# EX 0	0	1	3	
Accumulation, macrophage	0 0.00	0 0.00	1 2.00	3 3.00	

Severity Calculated by No. of Tissues Scored

(1) - 0 mg base/kg/day

(2) - 0.1 mg base/kg/day

(3) - 0.3 mg base/kg/day

(4) - 1.0 mg base/kg/day

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

SEVERITY SUMMARY

STUDY ID : TRL SN 193

STUDY NUMBER: 193

FATE: ALL

DAYS ON TEST: 184-184

SEX: FEMALE

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	4	4	4	4
	# SEV	# SEV	# SEV	# SEV
LUNG	# EX 4	4	4	4
Inflammation, chronic, interstitium	0 0.00	0 0.00	1 0.13	2 0.44
Atelectasis	0 0.00	0 0.00	1 0.31	0 0.00
Inflammation, chronic, peribronchial	0 0.00	0 0.00	0 0.00	1 0.06
SPLEEN	# EX 4	4	4	4
BONE MARROW (RIB)	# EX 4	4	4	4

Severity Calculated by No. of Tissues Scored

(1) - 0 mg base/kg/day

(2) - 0.1 mg base/kg/day

(3) - 0.3 mg base/kg/day

(4) - 1.0 mg base/kg/day

SECTION IV
TABULATED ANIMAL DATA

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

TABULATED ANIMAL DATA

STUDY ID : TRL SN 193	STUDY NUMBER: 193
FATE: ALL	GROUP: 1: 0 mg base/kg/day
DAYS ON TEST: ALL	SEX: MALE

ANIMAL ID:	8656	8669	8687	8673	8654	8667	8676	8680
BRAIN (FORE)	N	N	N	N				
SPINAL CORD (CERVICAL)	N	N	N					
Inflammation, chronic	-	-	-	(1)	-	-	-	-
BRAIN (MID)	N	N	N	N				
BRAIN (HIND)	N	N	N	N				
SPINAL CORD (THORACIC)	N	N	N	N				
HEART	N	N	N	N				
AORTA	N	N	N	N				
TRACHEA	N			N				
Inflammation, chronic	-	(1)	(1)	-	-	-	-	-
ESOPHAGUS	N	N	N	N				
LUNG	N	N	N	N	N	N	N	N
KIDNEY, RIGHT								
Mineralization, medulla	<1>	<1>	<1>	<1>	-	-	-	-
Infarction	-	-	(2)	-	-	-	-	-
Mineralization, cortex	-	-	(2)	-	-	-	-	-
KIDNEY, LEFT								
Mineralization, medulla	-	<1>	<1>	<1>	-	-	-	-
Inflammation, chronic	<1>	-	-	-	-	-	-	-
SPLEEN								
Siderotic nodule	(2)	-	-	-	-	-	-	-

See Reports Code Table for Symbol Definitions

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

TABULATED ANIMAL DATA

STUDY ID : TRL SN 193	STUDY NUMBER: 193							
FATE: ALL	GROUP: 1: 0 mg base/kg/day							
DAYS ON TEST: ALL	SEX: MALE							
ANIMAL ID:	8656	8669	8687	8673	8654	8667	8676	8680
PANCREAS	N	N	N	N				
DUODENUM	N	N	N	N				
LIVER								
Inflammation, chronic	<1>	-	<1>	<1>	-	-	-	-
Extramedullary hematopoiesis	<1>	<1>	-	-	-	-	-	-
GALLBLADDER			N					
Hyperplasia, lymphoid	<1>	<1>	-	(1)	-	-	-	-
ADRENAL GLAND	N	N	N	N				
SALIVARY GLAND	N	N	N	N				
LYMPH NODE, MANDIBULAR				N				
Hemorrhage	1	-	-	-	-	-	-	-
Pigmentation, macrophage	-	<1>	(1)	-	-	-	-	-
JEJUNUM	N	N	N	N				
COLON	N	N	N	N				
TONSIL	N	N	N	N				
ILEUM	N	N	N	N				
LYMPH NODE, MESENTERIC								
Hemorrhage	1	<1>	1	1	-	-	-	-
TONGUE	N	N	N	N				
DIAPHRAGM	N	N	N	N				
THYMUS	N	N	N	N				

See Reports Code Table for Symbol Definitions

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

TABULATED ANIMAL DATA

STUDY ID : TRL SM 193	STUDY NUMBER: 193
FATE: ALL	GROUP: 1: 0 mg base/kg/day
DAYS ON TEST: ALL	SEX: MALE

ANIMAL ID:	8656	8669	8687	8673	8654	8667	8676	8680
PROSTATE	N	N	N	N				
SKELETAL MUSCLE	N	N	N	N				
SKIN	N	N	N	N				
MAMMARY GLAND	N	N	N	N				
THYROID GLAND	N	N	N	N				
PARATHYROID GLAND	N	N	N	N				
PITUITARY GLAND		N	N	N				
Cyst	<1>	-	-	-	-	-	-	-
CECUM	N	N	N	N				
STOMACH				N				
Hyperplasia, lymphoid, submucosa	<1>	<1>	(1)	-	-	-	-	-
URINARY BLADDER	N	N	N	N				
TESTES	N	N	N	N				
SCIATIC NERVE	N	N	N	N				
URETER	N	N	N	N				
EYE	N	N	N	N				
OPTIC NERVE	N	N	N	N				
BONE MARROW (RIB)	N	N	N	N	N	N	N	N
BONE (RIB)	N	N	N	N				

See Reports Code Table for Symbol Definitions

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

TABULATED ANIMAL DATA

STUDY ID : TRL SN 193

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 193

GROUP: 2: 0.1 mg base/kg/day

SEX: MALE

ANIMAL ID:	8663	8677	8685	8686	8655	8659	8665	8666
BRAIN (FORE)	N	N	N	N				
SPINAL CORD (CERVICAL)	N	N	N	N				
BRAIN (MID)	N	N	N	N				
BRAIN (HIND)	N	N	N	N				
SPINAL CORD (THORACIC)	N	N	N	N				
HEART	N	N	N	N				
AORTA	N	N	N	N				
TRACHEA	N	N	N					
Inflammation, chronic	-	-	-	<1>	-	-	-	-
ESOPHAGUS	N	N	N	N				
LUNG	N	N	N	N	N	N	N	N
KIDNEY, RIGHT								
Mineralization, medulla	<1>	<1>	<2>	<1>	-	-	-	-
KIDNEY, LEFT		N						
Mineralization, medulla	<1>	-	<1>	<1>	-	-	-	-
SPLEEN	N	N	N	N	N	N	N	N
PANCREAS	N	N	N	N				
DUODENUM	N	N	N	N				
LIVER								
Inflammation, chronic	<1>	<1>	<1>	<1>	-	-	-	-

See Reports Code Table for Symbol Definitions

PATHOLOGY ASSOCIATES INTERNATIONAL
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
 WEEK RECOVERY PERIOD IN DOGS
 TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

TABULATED ANIMAL DATA

STUDY ID : TRL SN 193

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 193

GROUP: 2: 0.1 mg base/kg/day

SEX: MALE

ANIMAL ID:	8663	8677	8685	8686	8655	8659	8665	8666
LIVER								
Extramedullary hematopoiesis	<1>	<1>	<2>	-	-	-	-	-
GALLBLADDER		N	N	N				
Hyperplasia, lymphoid	(1)	-	-	-	-	-	-	-
ADRENAL GLAND	N	N	N	N				
SALIVARY GLAND	N	N		N				
Inflammation, chronic	-	-	(2)	-	-	-	-	-
LYMPH NODE, MANDIBULAR	N		N	N				
Pigmentation, macrophage	-	(1)	-	-	-	-	-	-
JEJUNUM	N	N	N	N				
COLON	N	N	N	N				
TONSIL	N	N	N	N				
ILEUM	N	N	N	N				
LYMPH NODE, MESENTERIC	N		N					
Hemorrhage	-	2	-	1	-	-	-	-
TONGUE	N	N	N	N				
DIAPHRAGM	N	N	N	N				
THYMUS	N	N	N	N				
PROSTATE	N	N	N	N				
SKELETAL MUSCLE	N	N	N	N				

See Reports Code Table for Symbol Definitions

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

TABULATED ANIMAL DATA

STUDY ID : TRL SN 193	STUDY NUMBER: 193
FATE: ALL	GROUP: 2: 0.1 mg base/kg/day
DAYS ON TEST: ALL	SEX: MALE

ANIMAL ID:	8663	8677	8685	8686	8655	8659	8665	8666
SKIN	N	N	N	N				
MAMMARY GLAND	N	N	N	N				
THYROID GLAND	N	N	N	N				
PARATHYROID GLAND	N	N	N	N				
PITUITARY GLAND			N					
Cyst	<1>	<1>	-	<1>	-	-	-	-
CECUM	N	N	N	N				
STOMACH								
Hyperplasia, lymphoid, submucosa	<1>	<1>	(1)	<1>	-	-	-	-
URINARY BLADDER	N	N	N	N				
TESTES	N	N	N	N				
SCIATIC NERVE	N	N	N	N				
URETER	N	N	N	N				
EYE	N	N	N	N				
OPTIC NERVE	N	N	N	N				
BONE MARROW (RIB)	N		N	N	N	N	N	N
Hyperplasia	-	1	-	-	-	-	-	-
BONE (RIB)	N	N	N	N				

See Reports Code Table for Symbol Definitions

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

TABULATED ANIMAL DATA

STUDY ID : TRL SN 193

STUDY NUMBER: 193

FATE: ALL

GROUP: 3: 0.3 mg base/kg/day

DAYS ON TEST: ALL

SEX: MALE

ANIMAL ID:	8653	8660	8668	8684	8662	8674	8682	8688
BRAIN (FORE)	N	N	N	N				
SPINAL CORD (CERVICAL)	N	N	N	N				
BRAIN (MID)	N	N	N	N				
BRAIN (HIND)	N	N	N	N				
SPINAL CORD (THORACIC)	N	N	N	N				
HEART	N	N	N	N				
AORTA	N	N	N	N				
TRACHEA				N				
Inflammation, chronic	(1)	(1)	(1)	-	-	-	-	-
ESOPHAGUS	N	N	N	N				
LUNG	N	N		N	N		N	N
Accumulation, alveolar macrophage	-	-	<>	-	-	(1)	-	-
Inflammation, chronic, perivascular	-	-	<>	-	-	-	-	-
Inflammation, chronic, interstitium	-	-	<1>	-	-	-	-	-
KIDNEY, RIGHT								
Mineralization, medulla	<1>	<1>	<>	<1>	-	-	-	-
Infarction	-	-	<>	-	-	-	-	-
Mineralization, cortex	-	-	<>	-	-	-	-	-
Eosinophilic casts	-	-	(1)	-	-	-	-	-
KIDNEY, LEFT								
Mineralization, medulla	<1>	<1>	<1>	<1>	-	-	-	-
Eosinophilic casts	-	-	<1>	-	-	-	-	-
Infarction	-	-	(3)	-	-	-	-	-

See Reports Code Table for Symbol Definitions

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

TABULATED ANIMAL DATA

STUDY ID : TRL SN 193

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 193

GROUP: 3: 0.3 mg base/kg/day

SEX: MALE

ANIMAL ID:	8653	8660	8668	8684	8662	8674	8682	8688
SPLEEN	N	N	N	N	N	N	N	N
PANCREAS	N	N	N	N				
DUODENUM	N	N	N	N				
LIVER								
Inflammation, chronic	<1>	<1>	<1>	<1>	-	-	-	-
Extramedullary hematopoiesis	<2>	<1>	-	<1>	-	-	-	-
GALLBLADDER	N	N						
Hyperplasia, lymphoid	-	-	<1>	<1>	-	-	-	-
ADRENAL GLAND	N	N	N	N				
SALIVARY GLAND	N	N		N				
Inflammation, chronic	-	-	(1)	-	-	-	-	-
LYMPH NODE, MANDIBULAR	N	N	N	N				
JEJUNUM	N	N	N	N				
COLON	N	N	N	N				
TONSIL	N	N	N	N				
ILEUM	N	N	N	N				
LYMPH NODE, MESENTERIC	N			N				
Hemorrhage	-	2	2	-	-	-	-	-
TONGUE	N	N	N	N				
DIAPHRAGM	N	N	N	N				

See Reports Code Table for Symbol Definitions

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

TABULATED ANIMAL DATA

STUDY ID : TRL SM 193

STUDY NUMBER: 193

FATE: ALL

GROUP: 3: 0.3 mg base/kg/day

DAYS ON TEST: ALL

SEX: MALE

ANIMAL ID:	8653	8660	8668	8684	8662	8674	8682	8688
THYMUS	N	N	N	N				
PROSTATE	N	N	N	N				
SKELETAL MUSCLE	N	N	N	N				
SKIN	N	N	N	N				
MAMMARY GLAND	N	N	N	N				
THYROID GLAND	N	N	N	N				
PARATHYROID GLAND	N	N	N	N				
PITUITARY GLAND		N		N				
Cyst	(1)	-	<1>	-	-	-	-	-
CECUM	N	N	N	N				
STOMACH	N							
Hyperplasia, lymphoid, submucosa	-	<>	<1>	<1>	-	-	-	-
URINARY BLADDER	N	N	N	N				
TESTES	N	N	N	N				
SCIATIC NERVE	N	N	N	N				
URETER	N	N	N	N				
EYE	N	N	N	N				
OPTIC NERVE	N	N	N	N				
BONE MARROW (RIB)					N	N	N	N

See Reports Code Table for Symbol Definitions

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

TABULATED ANIMAL DATA

STUDY ID : TRL SN 193

STUDY NUMBER: 193

FATE: ALL

GROUP: 3: 0.3 mg base/kg/day

DAYS ON TEST: ALL

SEX: MALE

ANIMAL ID:	8653	8660	8668	8684	8662	8674	8682	8688
BONE MARROW (RIB)					N	N	N	N
Hyperplasia	1	2	3	1	-	-	-	-
BONE (RIB)	N	N	N	N				

See Reports Code Table for Symbol Definitions

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

TABULATED ANIMAL DATA

STUDY ID : TRL SN 193

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 193

GROUP: 4: 1.0 mg base/kg/day

SEX: MALE

ANIMAL ID:	8661	8664	8670	8681	8652	8658	8675	8683
BRAIN (FORE)	N	N	N	N				
SPINAL CORD (CERVICAL)	N	N	N	N				
BRAIN (MID)	N	N	N	N				
BRAIN (HIND)	N	N	N	N				
SPINAL CORD (THORACIC)	N	N	N	N				
HEART	N	N	N	N				
AORTA	N	N	N	N				
TRACHEA	N		N	N				
Inflammation, chronic	-	(1)	-	-	-	-	-	-
ESOPHAGUS	N	N	N	N				
LUNG								N
Accumulation, alveolar macrophage	<2>	<3>	<3>	<3>	<1>	-	-	-
Inflammation, chronic, perivascular	<1>	<1>	<1>	<1>	<1>	-	-	-
Inflammation, chronic, interstitium	-	<2>	<1>	<1>	-	(1)	<1>	-
Basophilic granular material	-	-	<3>	-	-	-	-	-
KIDNEY, RIGHT								
Mineralization, medulla	<1>	<1>	<1>	<1>	-	-	-	-
KIDNEY, LEFT				N				
Mineralization, medulla	<1>	<2>	<1>	-	-	-	-	-
SPLEEN	N	N	N	N	N	N	N	N
PANCREAS	N	N	N	N				

See Reports Code Table for Symbol Definitions

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

TABULATED ANIMAL DATA

STUDY ID : TRL SN 193

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 193

GROUP: 4: 1.0 mg base/kg/day

SEX: MALE

ANIMAL ID:	8661	8664	8670	8681	8652	8658	8675	8683
DUODENUM	N	N	N	N				
LIVER								
Inflammation, chronic	<1>	<1>	<1>	<1>	-	-	-	-
Extramedullary hematopoiesis	<1>	<1>	-	<1>	-	-	-	-
GALLBLADDER								
Hyperplasia, lymphoid	(1)	<1>	<1>	(1)	-	-	-	-
ADRENAL GLAND	N	N	N	N				
SALIVARY GLAND								
Inflammation, chronic	-	-	-	(1)	-	-	-	-
LYMPH NODE, MANDIBULAR		N	N	N				
Pigmentation, macrophage	<2>	-	-	-	-	-	-	-
JEJUNUM	N	N	N	N				
COLON	N	N	N	N				
TONSIL	N	N	N	N				
ILEUM	N	N	N	N				
LYMPH NODE, MESENTERIC								
Hemorrhage	1	1	1	1	-	-	-	-
TONGUE	N	N	N	N				
DIAPHRAGM	N	N	N	N				
THYMUS	N	N	N	N				
PROSTATE	N	N	N	N				

See Reports Code Table for Symbol Definitions

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

TABULATED ANIMAL DATA

STUDY ID : TRL SN 193	STUDY NUMBER: 193
FATE: ALL	GROUP: 4: 1.0 mg base/kg/day
DAYS ON TEST: ALL	SEX: MALE

ANIMAL ID:	8661	8664	8670	8681	8652	8658	8675	8683
SKELETAL MUSCLE	N	N	N	N				
SKIN	N	N	N	N				
MAMMARY GLAND	N	U	N	U				
THYROID GLAND	N	N	N	N				
PARATHYROID GLAND	N	N	N	N				
PITUITARY GLAND			N	N				
Cyst	<1>	<1>	-	-	-	-	-	-
CECUM	N	N	N					
Cyst, crypt	-	-	-	(1)	-	-	-	-
STOMACH	N							
Hyperplasia, lymphoid, submucosa	-	<1>	<1>	<1>	-	-	-	-
URINARY BLADDER	N	N	N	N				
TESTES	N	N	N	N				
SCIATIC NERVE	N	N	N	N				
URETER	N	N	N	N				
EYE	N	N	N	N				
OPTIC NERVE	N	N	N	N				
BONE MARROW (RIB)					N	N	N	N
Hyperplasia	3	3	3	2	-	-	-	-
BONE (RIB)	N	N	N	N				

See Reports Code Table for Symbol Definitions

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

TABULATED ANIMAL DATA

STUDY ID : TRL SN 193

STUDY NUMBER: 193

FATE: ALL

GROUP: 4: 1.0 mg base/kg/day

DAYS ON TEST: ALL

SEX: MALE

ANIMAL ID:

8661 8664 8670 8681 8652 8658 8675 8683

LYMPH NODE, BRONCHIAL

Accumulation, macrophage

- 3 - 3 - - - -

See Reports Code Table for Symbol Definitions

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

TABULATED ANIMAL DATA

STUDY ID : TRL SN 193	STUDY NUMBER: 193							
FATE: ALL	GROUP: 1: 0 mg base/kg/day							
DAYS ON TEST: ALL	SEX: FEMALE							
ANIMAL ID:	8710	8712	8721	8723	8690	8699	8700	8705
BRAIN (FORE)	N	N	N	N				
SPINAL CORD (CERVICAL)	N	N	N	N				
BRAIN (MID)	N	N	N	N				
BRAIN (HIND)	N	N	N	N				
SPINAL CORD (THORACIC)	N	N	N	N				
HEART	N	N	N	N				
AORTA	N	N	N	N				
TRACHEA	N	N	N	N				
ESOPHAGUS	N	N	N					
Inflammation, chronic	-	-	-	(1)	-	-	-	-
LUNG		N			N	N	N	N
Accumulation, alveolar macrophage	-	-	<1>	(1)	-	-	-	-
Inflammation, chronic, perivascular	(1)	-	-	-	-	-	-	-
Inflammation, chronic, interstitium	-	-	<1>	-	-	-	-	-
KIDNEY, RIGHT	N							
Mineralization, medulla	-	<1>	<1>	<1>	-	-	-	-
KIDNEY, LEFT	N							
Mineralization, medulla	-	<1>	<1>	<1>	-	-	-	-
Mineralization, cortex	-	-	(1)	-	-	-	-	-
SPLEEN	N	N	N	N	N	N	N	N

See Reports Code Table for Symbol Definitions

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

TABULATED ANIMAL DATA

STUDY ID : TRL SN 193				STUDY NUMBER: 193				
FATE: ALL				GROUP: 1: 0 mg base/kg/day				
DAYS ON TEST: ALL				SEX: FEMALE				
ANIMAL ID:	8710	8712	8721	8723	8690	8699	8700	8705
PANCREAS	N	N	N	N				
DUODENUM	N	N	N	N				
LIVER								
Inflammation, chronic	-	<1>	<1>	<1>	-	-	-	-
Extramedullary hematopoiesis	<1>	<1>	<1>	<1>	-	-	-	-
GALLBLADDER			N					
Hyperplasia, lymphoid	(1)	<1>	-	<1>	-	-	-	-
ADRENAL GLAND	N	N	N	N				
SALIVARY GLAND	N	N	N	N				
LYMPH NODE, MANDIBULAR		N	N	N				
Hemorrhage	1	-	-	-	-	-	-	-
JEJUNUM	N	N	N	N				
COLON	N	N	N	N				
TONSIL	N	N	N	N				
ILEUM	N	N	N	N				
LYMPH NODE, MESENTERIC		N	N					
Hemorrhage	2	-	-	1	-	-	-	-
TONGUE	N	N	N	N				
DIAPHRAGM	N	N	N	N				
THYMUS	N	N	N	N				

See Reports Code Table for Symbol Definitions

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

TABULATED ANIMAL DATA

STUDY ID : TRL SN 193	STUDY NUMBER: 193							
FATE: ALL	GROUP: 1: 0 mg base/kg/day							
DAYS ON TEST: ALL	SEX: FEMALE							
ANIMAL ID:	8710	8712	8721	8723	8690	8699	8700	8705
SKELETAL MUSCLE	N	N	N	N				
SKIN	N	N	N	N				
MAMMARY GLAND	N	N	N					
Lactation	-	-	-	P	-	-	-	-
THYROID GLAND			N	N				
Cyst	(2)	(1)	-	-	-	-	-	-
PARATHYROID GLAND	N	N	N	N				
PITUITARY GLAND			N					
Cyst	<1>	(3)	-	<2>	-	-	-	-
CECUM	N	N	N	N				
STOMACH								
Hyperplasia, lymphoid, submucosa	<2>	<1>	<2>	<1>	-	-	-	-
URINARY BLADDER	N	N	N	N				
OVARY	N	N						
Cyst	-	-	(2)	-	-	-	-	-
Corpora lutea	-	-	-	P	-	-	-	-
UTERUS	N	N	N	N				
SCIATIC NERVE	N	N	N	N				
URETER	N	N	N	N				
EYE	N	N	N	N				
OPTIC NERVE:	N	N	N	N				

See Reports Code Table for Symbol Definitions

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

TABULATED ANIMAL DATA

STUDY ID : TRL SN 193

STUDY NUMBER: 193

FATE: ALL

GROUP: 1: 0 mg base/kg/day

DAYS ON TEST: ALL

SEX: FEMALE

ANIMAL ID:	8710	8712	8721	8723	8690	8699	8700	8705
BONE MARROW (RIB)	N	N	N	N	N	N	N	N
BONE (RIB)	N	N	N	N				

See Reports Code Table for Symbol Definitions

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

TABULATED ANIMAL DATA

STUDY ID : TRL SN 193	STUDY NUMBER: 193							
FATE: ALL	GROUP: 2: 0.1 mg base/kg/day							
DAYS ON TEST: ALL	SEX: FEMALE							
ANIMAL ID:	8693	8703	8713	8717	8695	8697	8709	8715
BRAIN (FORE)	N	N	N	N				
SPINAL CORD (CERVICAL)	N	N	N	N				
BRAIN (MID)	N	N	N	N				
BRAIN (HIND)	N	N	N	N				
SPINAL CORD (THORACIC)	N	N	N	N				
HEART	N	N		N				
Degeneration, mucoid, valve	-	-	[2]	-	-	-	-	-
AORTA	N	N	N	N				
TRACHEA	N	N						
Inflammation, chronic	-	-	(1)	(1)	-	-	-	-
ESOPHAGUS	N	N	N	N				
LUNG	N				N	N	N	N
Accumulation, alveolar macrophage	-	(1)	(1)	-	-	-	-	-
Inflammation, chronic, perivascular	-	-	<1>	<1>	-	-	-	-
KIDNEY, RIGHT								
Mineralization, medulla	<1>	<1>	<1>	<1>	-	-	-	-
Inflammation, chronic	(1)	-	-	-	-	-	-	-
KIDNEY, LEFT								
Mineralization, medulla	<1>	<1>	<1>	<1>	-	-	-	-
SPLEEN	N	N	N	N	N	N	N	N
PANCREAS	N	N	N	N				

See Reports Code Table for Symbol Definitions

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

TABULATED ANIMAL DATA

STUDY ID : TRL SN 193	STUDY NUMBER: 193							
FATE: ALL	GROUP: 2: 0.1 mg base/kg/day							
DAYS ON TEST: ALL	SEX: FEMALE							
ANIMAL ID:	8693	8703	8713	8717	8695	8697	8709	8715
DUODENUM	N	N	N	N				
LIVER								
Inflammation, chronic	<1>	<1>	<1>	<1>	-	-	-	-
Extramedullary hematopoiesis	-	<1>	<1>	-	-	-	-	-
GALLBLADDER	N							
Hyperplasia, lymphoid	-	<1>	<1>	(1)	-	-	-	-
ADRENAL GLAND	N	N	N	N				
SALIVARY GLAND	N	N	N	N				
LYMPH NODE, MANDIBULAR		N	N	N				
Pigmentation, macrophage	<1>	-	-	-	-	-	-	-
JEJUNUM	N	N	N	N				
COLON	U	N	N	N				
TONSIL		N	N	N				
Bacterial colony	(2)	-	-	-	-	-	-	-
ILEUM	U	N	N	N				
LYMPH NODE, MESENTERIC	N			N				
Hemorrhage	-	1	2	-	-	-	-	-
TONGUE	N	N	N	N				
DIAPHRAGM	N	N	N	N				
THYMUS	N	N	N	N				
SKELETAL MUSCLE	N	N	N	N				

See Reports Code Table for Symbol Definitions

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PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

TABULATED ANIMAL DATA

STUDY ID : TRL SN 193

STUDY NUMBER: 193

FATE: ALL

GROUP: 2: 0.1 mg base/kg/day

DAYS ON TEST: ALL

SEX: FEMALE

ANIMAL ID:	8693	8703	8713	8717	8695	8697	8709	8715
SKIN	N	N	N	N				
MAMMARY GLAND	N	N	N	N				
THYROID GLAND	N	N	N	N				
PARATHYROID GLAND	N	N	N	N				
PITUITARY GLAND	N		N					
Cyst	-	<1>	-	<2>	-	-	-	-
CECUM	U	N	N	N				
STOMACH								
Hyperplasia, lymphoid, submucosa	<1>	<1>	<1>	<1>	-	-	-	-
URINARY BLADDER	N	N	N	N				
OVARY		N		N				
Cyst	(2)	-	-	-	-	-	-	-
Corpora lutea	P	-	P	-	-	-	-	-
UTERUS	N	N	N	N				
SCIATIC NERVE	N	N	N	N				
URETER	N	N	N	N				
EYE	N	N	N	N				
OPTIC NERVE	N	N	N	N				
BONE MARROW (RIB)	N	N	N	N	N	N	N	N
BONE (RIB)	N	N	N	N				

See Reports Code Table for Symbol Definitions

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

TABULATED ANIMAL DATA

STUDY ID : TRL SN 193	STUDY NUMBER: 193						
FATE: ALL	GROUP: 3: 0.3 mg base/kg/day						
DAYS ON TEST: ALL	SEX: FEMALE						
ANIMAL ID:	8692	8706	8714 - 8718	8701	8702	8704	8720
BRAIN (FORE)	N	N	N	N			
SPINAL CORD (CERVICAL)	N	N	N	N			
BRAIN (MID)	N	N	N	N			
BRAIN (HIND)	N	N	N	N			
SPINAL CORD (THORACIC)	N	N	N	N			
HEART		N	N	N			
Degeneration, mucoid, valve	[2]	-	-	-	-	-	-
AORTA	N	N	N	N			
TRACHEA	N	N		N			
Inflammation, chronic	-	-	<1>	-	-	-	-
ESOPHAGUS	N	N	N	N			
LUNG	N		N			N	N
Accumulation, alveolar macrophage	-	<3>	-	<1>	-	-	-
Inflammation, chronic, perivascular	-	<2>	-	<1>	-	-	-
Inflammation, chronic, interstitium	-	<2>	-	-	-	<1>	-
Atelectasis	-	-	-	-	(2)	-	-
KIDNEY, RIGHT							
Mineralization, medulla	<2>	<1>	<1>	<1>	-	-	-
KIDNEY, LEFT							
Mineralization, medulla	-	<1>	<2>	<1>	-	-	-
Eosinophilic casts	(2)	-	-	-	-	-	-
Infarction	(2)	-	-	-	-	-	-
SPLEEN		N		N	N	N	N

See Reports Code Table for Symbol Definitions

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

TABULATED ANIMAL DATA

STUDY ID : TRL SN 193				STUDY NUMBER: 193				
FATE: ALL				GROUP: 3: 0.3 mg base/kg/day				
DAYS ON TEST: ALL				SEX: FEMALE				
ANIMAL ID:	8692	8706	8714	8718	8701	8702	8704	8720
SPLEEN		N		N	N	N	N	N
Erythropoiesis	1	-	1	-	-	-	-	-
PANCREAS	N	N	N	N				
DUODENUM	N	N	N	N				
LIVER								
Inflammation, chronic	<1>	<1>	<1>	<1>	-	-	-	-
Extramedullary hematopoiesis	<1>	<1>	<1>	<1>	-	-	-	-
GALLBLADDER	N			N				
Hyperplasia, lymphoid	-	(1)	<>	-	-	-	-	-
ADRENAL GLAND	N	N	N	N				
SALIVARY GLAND	N	N	N	N				
LYMPH NODE, MANDIBULAR			N	N				
Pigmentation, macrophage	(1)	<1>	-	-	-	-	-	-
JEJUNUM	N	N	N	N				
COLON	N	N	N	N				
TONSIL	N	N	N	N				
ILEUM	N	N	N	N				
LYMPH NODE, MESENTERIC								
Hemorrhage:	1	1	1	1	-	-	-	-
TONGUE	N	N	N	N				
DIAPHRAGM	N	N	N	N				

See Reports Code Table for Symbol Definitions

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

TABULATED ANIMAL DATA

STUDY ID : TRL SN 193	STUDY NUMBER: 193							
FATE: ALL	GROUP: 3: 0.3 mg base/kg/day							
DAYS ON TEST: ALL	SEX: FEMALE							
ANIMAL ID:	8692	8706	8714	8718	8701	8702	8704	8720
THYMUS	N	N	N	N				
SKELETAL MUSCLE	N	N	N	N				
SKIN	N	N	N	N				
MAMMARY GLAND		N	N					
Lactation	P	-	-	P	-	-	-	-
THYROID GLAND	N	N	N	N				
PARATHYROID GLAND	N	N	N	N				
PITUITARY GLAND		N	N	N				
Cyst	(2)	-	-	-	-	-	-	-
CECUM	N		N	N				
Cyst, crypt	-	(1)	-	-	-	-	-	-
STOMACH	N							
Hyperplasia, lymphoid, submucosa	-	<1>	<1>	2	-	-	-	-
URINARY BLADDER	N	N	N	N				
OVARY		N						
Corpora lutea	P	-	P	P	-	-	-	-
UTERUS	N	N	N	N				
SCIATIC NERVE	N	N	N	N				
URETER	N	N	N	N				
EYE	N	N	N	N				

See Reports Code Table for Symbol Definitions

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

TABULATED ANIMAL DATA

STUDY ID : TRL SN 193

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 193

GROUP: 3: 0.3 mg base/kg/day

SEX: FEMALE

ANIMAL ID:	8692	8706	8714	8718	8701	8702	8704	8720
OPTIC NERVE	N	N	N	N				
BONE MARROW (RIB)		N	N		N	N	N	N
Hyperplasia	1	-	-	1	-	-	-	-
BONE (RIB)	N	N	N	N				
LYMPH NODE, BRONCHIAL								
Accumulation, macrophage	-	2	-	-	-	-	-	-

See Reports Code Table for Symbol Definitions

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

TABULATED ANIMAL DATA

STUDY ID : TRL SN 193				STUDY NUMBER: 193				
FATE: ALL				GROUP: 4: 1.0 mg base/kg/day				
DAYS ON TEST: ALL				SEX: FEMALE				
ANIMAL ID:	8696	8711	8716	8719	8689	8722	8707	8725
BRAIN (FORE)	N	N	N	N				
SPINAL CORD (CERVICAL)	N	N	N	N				
BRAIN (MID)	N		N	N				
Inflammation, chronic	-	(1)	-	-	-	-	-	-
BRAIN (HIND)	N	N	N	N				
SPINAL CORD (THORACIC)	N	N	N	N				
HEART	N	N	N	N				
AORTA	N	N	N	N				
TRACHEA	N	N	N	N				
ESOPHAGUS	N	N	N	N				
LUNG					N			
Accumulation, alveolar macrophage	<2>	<3>	<3>	<3>	-	-	-	-
Inflammation, chronic, perivascular	<1>	<1>	<2>	<1>	-	-	-	-
Inflammation, chronic, interstitium	<2>	<2>	<2>	<2>	-	<1>	(2)	-
Basophilic granular material	-	[3]	<1>	<1>	-	-	-	-
Inflammation, chronic, peribronchial	-	-	-	-	-	-	-	(1)
KIDNEY, RIGHT		N						
Mineralization, medulla	<1>	-	<1>	<1>	-	-	-	-
KIDNEY, LEFT								
Mineralization, medulla	<1>	<1>	<1>	<1>	-	-	-	-
SPLEEN	N			N	N	N	N	N
Erythropoiesis	-	1	2	-	-	-	-	-

See Reports Code Table for Symbol Definitions

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

TABULATED ANIMAL DATA

STUDY ID : TRL SN 193

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 193

GROUP: 4: 1.0 mg base/kg/day

SEX: FEMALE

ANIMAL ID:	8696	8711	8716	8719	8689	8722	8707	8725
PANCREAS	N	N	N	N				
DUODENUM	N	N	N	N				
LIVER								
Inflammation, chronic	<1>	-	-	<1>	-	-	-	-
Extramedullary hematopoiesis	<2>	<1>	<2>	<1>	-	-	-	-
GALLBLADDER	N							
Hyperplasia, lymphoid	-	(1)	<1>	(1)	-	-	-	-
ADRENAL GLAND	N	N	N	N				
SALIVARY GLAND	N	N	N	N				
LYMPH NODE, MANDIBULAR			N	N				
Hemorrhage	1	-	-	-	-	-	-	-
Pigmentation, macrophage	-	<1>	-	-	-	-	-	-
JEJUNUM	N	N	N	N				
COLON	N	N	N	N				
TONSIL	U	N	N					
Bacterial colony	-	-	-	(4)	-	-	-	-
ILEUM	N	N	N	N				
LYMPH NODE, MESENTERIC		N	N					
Hemorrhage	1	-	-	1	-	-	-	-
TONGUE	N	N	N	N				
DIAPHRAGM	N	N	N	N				

See Reports Code Table for Symbol Definitions

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

TABULATED ANIMAL DATA

STUDY ID : TRL SN 193

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 193

GROUP: 4: 1.0 mg base/kg/day

SEX: FEMALE

ANIMAL ID:	8696	8711	8716	8719	8689	8722	8707	8725
THYMUS	N	N	N	N				
SKELETAL MUSCLE	N	N	N	N				
SKIN	N	N	N	N				
MAMMARY GLAND Lactation	N	N	N					
	-	-	-	P	-	-	-	-
THYROID GLAND	N	N	N	N				
PARATHYROID GLAND Cyst	N	N	N					
	-	-	-	(2)	-	-	-	-
PITUITARY GLAND Cyst		N		N				
	<3>	-	(1)	-	-	-	-	-
CECUM	N	N	N	N				
STOMACH Hyperplasia, lymphoid, submucosa	<1>	<2>	<1>	<1>	-	-	-	-
URINARY BLADDER	N	N	N	N				
OVARY Corpora lutea	N	N	N					
	-	-	-	P	-	-	-	-
UTERUS	N	N	N	N				
SCIATIC NERVE	N	N	N	N				
URETER	N	N	N	N				
EYE	N	N	N	N				

See Reports Code Table for Symbol Definitions

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

TABULATED ANIMAL DATA

STUDY ID : TRL SN 193

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 193

GROUP: 4: 1.0 mg base/kg/day

SEX: FEMALE

ANIMAL ID:	8696	8711	8716 . 8719	8689	8722	8707	8725
OPTIC NERVE	N	N	N	N			
BONE MARROW (RIB)					N	N	N
Hyperplasia	2	1	2	1	-	-	-
BONE (RIB)	N	N	N	N			
LYMPH NODE, BRONCHIAL							
Accumulation, macrophage	-	3	3	3	-	-	-

See Reports Code Table for Symbol Definitions

SECTION V
CORRELATION OF GROSS AND MICROSCOPIC (MICRO) FINDINGS

DEAFY

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PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

CORRELATION OF GROSS & MICRO

STUDY ID : TRL SN 193

STUDY NUMBER: 193

FATE: ALL

GROUP: 1: 0 mg base/kg/day

DAYS ON TEST: ALL

SEX: MALE

Animal ID: 8680

Animal Fate: Scheduled sacrifice

Days on Test: 183

Reference to Necropsy Record:

PITUITARY GLAND - CYST, 5 MM DIAMETER, CLEAR

Related Histopathology:

PITUITARY GLAND - Not required by protocol

DRAFT

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PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

CORRELATION OF GROSS & MICRO

STUDY ID : TRL SN 193

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 193

GROUP: 2: 0.1 mg base/kg/day

SEX: MALE

No Gross Observations for any animal in this group

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

CORRELATION OF GROSS & MICRO

STUDY ID : TRL SN 193

STUDY NUMBER: 193

FATE: ALL

GROUP: 3: 0.3 mg base/kg/day

DAYS ON TEST: ALL

SEX: MALE

Animal ID: 8668

Animal Fate: Scheduled sacrifice

Days on Test: 92

Reference to Necropsy Record:

KIDNEY, RIGHT - DEFORMITY, MULTIPLE

KIDNEY, LEFT - DEFORMITY, MULTIPLE

Related Histopathology:

KIDNEY, RIGHT - Infarction

KIDNEY, LEFT - Infarction

Animal ID: 8662

Animal Fate: Scheduled sacrifice

Days on Test: 183

Reference to Necropsy Record:

THYMUS - PIGMENTATION, RED

Related Histopathology:

THYMUS - Not required by protocol

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

CORRELATION OF GROSS & MICRO

STUDY ID : TRL SN 193

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 193

GROUP: 4: 1.0 mg base/kg/day

SEX: MALE

Animal ID: 8661

Animal Fate: Scheduled sacrifice

Days on Test: 92

Reference to Necropsy Record:

LUNG - FOCUS, 1 MM X 1 MM, MULTIPLE, WHITE

Related Histopathology:

LUNG - Accumulation, alveolar macrophage

Animal ID: 8664

Animal Fate: Scheduled sacrifice

Days on Test: 92

Reference to Necropsy Record:

LUNG - FOCUS, 1 MM X 1 MM, MULTIPLE, WHITE

Related Histopathology:

LUNG - Accumulation, alveolar macrophage

LYMPH NODE, BRONCHIAL - ENLARGED, 12 MM X 10 MM,
MOTTLED

LYMPH NODE, BRONCHIAL - Accumulation, macrophage

Animal ID: 8670

Animal Fate: Scheduled sacrifice

Days on Test: 92

Reference to Necropsy Record:

LUNG - BILATERAL, FOCUS, MULTIPLE, WHITE

Related Histopathology:

LUNG - Accumulation, alveolar macrophage

Animal ID: 8681

Animal Fate: Scheduled sacrifice

Days on Test: 92

Reference to Necropsy Record:

LUNG - FOCUS, 1 MM X 1 MM, MULTIPLE, WHITE

Related Histopathology:

LUNG - Accumulation, alveolar macrophage

LYMPH NODE, BRONCHIAL - ENLARGED, 12 MM X 10 MM,
MOTTLED

LYMPH NODE, BRONCHIAL - Accumulation, macrophage

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

CORRELATION OF GROSS & MICRO

STUDY ID : TRL SN 193

STUDY NUMBER: 193

FATE: ALL

GROUP: 4: 1.0 mg base/kg/day

DAYS ON TEST: ALL

SEX: MALE

Animal ID: 8658

Animal Fate: Scheduled sacrifice

Days on Test: 183

Reference to Necropsy Record:

PITUITARY GLAND - CYST, 5 MM DIAMETER, CLEAR

Related Histopathology:

PITUITARY GLAND - Not required by protocol

DRAFT

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PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

CORRELATION OF GROSS & MICRO

STUDY ID : TRL SN 193

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 193

GROUP: 1: 0 mg base/kg/day

SEX: FEMALE

No Gross Observations for any animal in this group

DRAFT

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PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

CORRELATION OF GROSS & MICRO

STUDY ID : TRL SN 193

STUDY NUMBER: 193

FATE: ALL

GROUP: 2: 0.1 mg base/kg/day

DAYS ON TEST: ALL

SEX: FEMALE

Animal ID: 8695

Animal Fate: Scheduled sacrifice

Days on Test: 184

Reference to Necropsy Record:

Related Histopathology:

TONSIL - BILATERAL, PIGMENTATION, RED

TONSIL - Not required by protocol

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

CORRELATION OF GROSS & MICRO

STUDY ID : TRL SN 193

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 193

GROUP: 3: 0.3 mg base/kg/day

SEX: FEMALE

Animal ID: 8706

Animal Fate: Scheduled sacrifice

Days on Test: 93

Reference to Necropsy Record:

LUNG - FOCUS, 1 MM X 1 MM, MULTIPLE, WHITE

Related Histopathology:

LUNG - Accumulation, alveolar macrophage

LYMPH NODE, BRONCHIAL - ENLARGED, 20 MM X 10 MM X 3
MM, MOTTLED

LYMPH NODE, BRONCHIAL - Accumulation, macrophage

Animal ID: 8701

Animal Fate: Scheduled sacrifice

Days on Test: 184

Reference to Necropsy Record:

LUNG - LEFT APICAL LOBE, DEFORMITY

Related Histopathology:

LUNG - Atelectasis

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

CORRELATION OF GROSS & MICRO

STUDY ID : TRL SN 193

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 193

GROUP: 4: 1.0 mg base/kg/day

SEX: FEMALE

Animal ID: 8711

Animal Fate: Scheduled sacrifice

Days on Test: 93

Reference to Necropsy Record:

LUNG - FOCUS, 1 MM X 1 MM, WHITE, MULTIPLE

LYMPH NODE, BRONCHIAL - ENLARGED, 10 MM X 12 MM

Related Histopathology:

LUNG - Accumulation, alveolar macrophage

LYMPH NODE, BRONCHIAL - Accumulation, macrophage

Animal ID: 8716

Animal Fate: Scheduled sacrifice

Days on Test: 93

Reference to Necropsy Record:

LUNG - FOCUS, 1 MM X 1 MM, WHITE, MULTIPLE

LYMPH NODE, BRONCHIAL - ENLARGED, 10 MM X 12 MM,
MOTTLED

Related Histopathology:

LUNG - Accumulation, alveolar macrophage

LYMPH NODE, BRONCHIAL - Accumulation, macrophage

Animal ID: 8719

Animal Fate: Scheduled sacrifice

Days on Test: 93

Reference to Necropsy Record:

LUNG - FOCUS, 1 MM X 1 MM, MULTIPLE, WHITE

LYMPH NODE, BRONCHIAL - ENLARGED, 15 MM X 10 MM X 3
MM, MOTTLED

Related Histopathology:

LUNG - Accumulation, alveolar macrophage

LYMPH NODE, BRONCHIAL - Accumulation, macrophage

PATHOLOGY ASSOCIATES INTERNATIONAL
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN
WEEK RECOVERY PERIOD IN DOGS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 193

CORRELATION OF GROSS & MICRO

STUDY ID : TRL SN 193

STUDY NUMBER: 193

FATE: ALL

GROUP: 4: 1.0 mg base/kg/day

DAYS ON TEST: ALL

SEX: FEMALE

Animal ID: 8707

Animal Fate: Scheduled sacrifice

Days on Test: 184

Reference to Necropsy Record:

Related Histopathology:

LUNG - RIGHT APICAL LOBE, PIGMENTATION, 15 MM X 15
MM, GREY

LUNG - No corresponding lesion

LUNG - LEFT APICAL LOBE, PIGMENTATION, 10 MM X 10
MM, WHITE

LUNG - Inflammation, chronic, interstitium

SECTION VI
QUALITY ASSURANCE STATEMENT

QUALITY ASSURANCE STATEMENT

This histopathology project was inspected and audited by the PAI Quality Assurance Unit (QAU) as required by the Good Laboratory Practice (GLP) standards promulgated by the U.S. Food and Drug Administration. The pathology narrative report is an accurate reflection of the recorded data. The following table is a record of the inspections/audits performed and reported by the QAU:

Date of Inspection	Phase Inspected	Date Findings Reported to Management and Study Pathologist
* 11/08/95	Tissue Trimming	11/08/95
** 01/05/96	Processing/Embedding	01/05/96
* 03/27/96	Microtomy	03/28/96
* 12/29/95	Staining	12/29/95
* 12/29/95	Coverslipping	12/29/95
* 05/13/96	Labeling	05/13/96
* 11/16/95	Quality Control/Checkout	11/16/95
** 05/17/96	Individual Animal Data	05/17/96
** 05/17/96	Draft Pathology Report	05/17/96
** 05/23/96	Revised Draft Pathology Report	05/23/96

* General quarterly phase inspection

** Inspection specific for this study

In accordance with the PAI Quality Assurance Division's Standard Operating Procedures, all critical phase inspections are conducted on a random basis quarterly or more frequently. Those general phase inspections listed are the most recent conducted during the period each task associated with this project was performed.



Andrea M. Smith
Quality Assurance Unit
PAI Illinois Division

05/23/96

Date

Thirteen Week Oral Toxicity Study of WR242511 with a Thirteen Week Recovery Period in Dogs
UIC/TRL Study Number 193

SECTION VII
BONE MARROW EVALUATION REPORT



BONE MARROW EVALUATION REPORT
FOR

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

TRL STUDY NUMBER 193

PREPARED FOR
TOXICOLOGY RESEARCH LABORATORY

L-80

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Individual Animal M:E Ratio Tables	89
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I. Bone Marrow Evaluation Narrative

BONE MARROW EVALUATION REPORT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INTRODUCTION

This report prepared by Pathology Associates International (PAI) for Toxicology Research Laboratory (UIC/TRL), University of Illinois at Chicago, Department of Pharmacology, 1940 West Taylor Street, Chicago, IL, 60612-7353, presents the results of bone marrow evaluation from dogs given WR242511 orally, once per day, for at least thirteen weeks.

EXPERIMENTAL DESIGN AND METHODS

Thirty-two male and thirty-two female dogs were randomized into one of four groups as described below.

Treatment Group	Dose Level (mg base/kg/day)	Number of Males	Number of Females
1	0.0	4 + 4*	4 + 4*
2	0.1	4 + 4*	4 + 4*
3	0.3	4 + 4*	4 + 4*
4	1.0	4 + 4*	4 + 4*

*Recovery Animals.

Four animals per sex in each dose groups were necropsied during Week 14. The remainder of the animals were held for a thirteen week recovery period at which time they were necropsied.

Bone marrow smears were prepared from the rib of each animal at the Week 14 necropsy. The smears were fixed in methanol, stained with a Wrights-Giemsa stain, and evaluated microscopically to determine the Myeloid:Erythroid (M:E) Ratio. The M:E Ratio was determined on a cell count of 500 cells.

Statistical analysis of the data was performed by UIC/TRL and provided to PAI for inclusion in this report.

RESULTS

M:E Ratio Group Summary tables are presented in Section II (generated by UIC/TRL from PAI data sheets). Individual animal M:E Ratio data are presented by dose group and sex in Section III (generated by UIC/TRL from PAI data sheets).

The M:E Ratios from bone marrow smears collected during Week 14 in this study indicated a decrease in the M:E Ratios in male and female dogs receiving 1.0 mg base/kg/day. This decrease was statistically significant in the female dogs. For this reason, bone marrow was evaluated from the recovery animals during Week 27. The M:E Ratios from bone marrow smears collected from these animals were all considered to be within normal limits.

CONCLUSION

Under the conditions of this study, WR242511 resulted in a treatment-related decrease in the M:E Ratio of the rib bone marrow of male and female dogs treated with 1.0 mg base/kg/day at Week 14. The M:E Ratios from male and female dogs after the recovery period (Week 27) were all considered to be within normal limits.

Lynda L. Lanning, D.V.M., D.A.B.T.
May 17, 1996

II. M:E Ratio Summary Tables

THIRTEEN WEEK ORAL TOXICITY STUDY
OF WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

SUMMARY REPORT
TEST: M:E RATIO

STUDY ID: 193
STUDY NO: 193ME
ABBR: M:E RATIO

SEX: MALE

UNITS: -

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

GROUP(s): 1-M 2-M 3-M 4-M

Period: Week 14

MEAN	1.20	1.19	1.23	1.10
SD	0.052	0.050	0.046	0.059
N	4	4	4	4

Period: Week 27

MEAN	1.15	1.15	1.23	1.16
SD	0.066	0.118	0.091	0.062
N	4	4	4	4

THIRTEEN WEEK ORAL TOXICITY STUDY
OF WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

SUMMARY REPORT
TEST: M:E RATIO

STUDY ID: 193
STUDY NO: 193ME
ABBR: M:E RATIO

SEX: FEMALE

UNITS: -

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

GROUP(s):	1-F	2-F	3-F	4-F
Period: Week 14				
MEAN	1.23	1.23	1.16	1.08*
SD	0.053	0.064	0.070	0.047
N	4	4	4	4
Period: Week 27				
MEAN	1.25	1.26	1.28	1.25
SD	0.059	0.070	0.079	0.077
N	4	4	4	4

*-Significant Difference from Control P < .05

THIRTEEN WEEK ORAL TOXICITY STUDY
OF WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

SUMMARY REPORT
TEST: M:E RATIO

STUDY ID: 193
STUDY NO: 193ME
ABBR: M:E RATIO

SEX: MALE

UNITS: -

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 14

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES				Source	Degree of Freedom	Sum of Squares	Mean Square
1-M	4	4.78	1.20	0.052						TREATMENTS	3	0.0379	0.0126
2-M	4	4.76	1.19	0.050	0.14	1.00	1.00	1.00	1.00	ERROR	12	0.0324	0.0027
3-M	4	4.93	1.23	0.046	1.02	1.00	1.00	1.00	1.00				
4-M	4	4.40	1.10	0.059	2.59	1.00	1.00	1.00	1.00	TOTAL	15	0.0703	
F Ratio =				4.68	'F' table values				F.01 =	5.95	F.05 =	3.49	
Coeff. Var. % =				4.404	Dunnett's 'T' table values				P.01 =	3.58	P.05 =	2.68	

Week 27

1-M	4	4.58	1.15	0.066						TREATMENTS	3	0.0191	0.0064
2-M	4	4.60	1.15	0.118						ERROR	12	0.0916	0.0076
3-M	4	4.92	1.23	0.091									
4-M	4	4.63	1.16	0.062						TOTAL	15	0.1107	
F Ratio =				0.84	'F' table values				F.01 =	5.95	F.05 =	3.49	
Coeff. Var. % =				7.462	Dunnett's 'T' table values				P.01 =	3.58	P.05 =	2.68	

Error-within groups
Source-Source of Variation

Treatments-between groups

THIRTEEN WEEK ORAL TOXICITY STUDY
OF WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

SUMMARY REPORT
TEST: M:E RATIO

STUDY ID: 193
STUDY NO: 193ME
ABBR: M:E RATIO

SEX: FEMALE

UNITS: -

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 14

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES				Source	Degree of Freedom	Sum of Squares	Mean Square
1-F	4	4.91	1.23	0.053						TREATMENTS	3	0.0590	0.0197
2-F	4	4.91	1.23	0.064	0.00	1.00	1.00	1.00	1.00	ERROR	12	0.0420	0.0035
3-F	4	4.64	1.16	0.070	1.61	1.00	1.00	1.00	1.00				
4-F	4	4.32	1.08	0.047	3.53	1.00	1.00*	1.00	1.00	TOTAL	15	0.1010	

F Ratio = 5.63 'F' table values F.01 = 5.95 F.05 = 3.49
Coeff. Var. % = 5.037 Dunnett's 'T' table values P.01 = 3.58 P.05 = 2.68

Week 27

1-F	4	5.01	1.25	0.059						TREATMENTS	3	0.0027	0.0009
2-F	4	5.04	1.26	0.070						ERROR	12	0.0616	0.0051
3-F	4	5.12	1.28	0.079									
4-F	4	4.98	1.25	0.077						TOTAL	15	0.0643	

F Ratio = 0.18 'F' table values F.01 = 5.95 F.05 = 3.49
Coeff. Var. % = 5.688 Dunnett's 'T' table values P.01 = 3.58 P.05 = 2.68

*-Significant Difference from Control P < .05
Error-within groups

Source-Source of Variation
Treatments-between groups

III. Individual Animal M:E Ratio Tables

THIRTEEN WEEK ORAL TOXICITY STUDY
OF WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: M:E RATIO

STUDY ID: 193
STUDY NO: 193ME
ABBR: M:E RATIO

SEX: MALE

UNITS: -

Animal ID Week 14 Week 27

GROUP: 1-M:0 mg base/kg/day

8656	1.21	--
8687	1.26	--
8669	1.17	--
8673	1.14	--
8667	--	1.22
8654	--	1.16
8680	--	1.06
8676	--	1.14
---	---	---
MEAN	1.20	1.15
SD	0.052	0.066
N	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY
OF WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: M:E RATIO

STUDY ID: 193
STUDY NO: 193ME
ABBR: M:E RATIO

SEX: MALE

UNITS: -

Animal ID Week 14 Week 27

GROUP: 2-M:0.1 mg base/kg/day

8685	1.19	--
8663	1.15	--
8686	1.26	--
8665	--	1.26
8666	--	1.24
8655	--	1.08
8659	--	1.02
8677	1.16	--

MEAN	1.19	1.15
.SD	0.050	0.118
N	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY
OF WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: M:E RATIO

STUDY ID: 193
STUDY NO: 193ME
ABBR: M:E RATIO

SEX: MALE

UNITS: -

Animal ID	Week 14	Week 27
-----------	---------	---------

GROUP: 3-M:0.3 mg base/kg/day		
8674	--	1.18
8653	1.28	--
8660	1.23	--
8668	1.25	--
8682	--	1.28
8684	1.17	--
8662	--	1.33
8688	--	1.13
MEAN	1.23	1.23
SD	0.046	0.091
N	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY
OF WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: M:E RATIO

STUDY ID: 193
STUDY NO: 193ME
ABBR: M:E RATIO

SEX: MALE

UNITS: -

Animal ID Week 14 Week 27

GROUP: 4-M:1.0 mg base/kg/day

8661	1.10	--
8670	1.18	--
8681	1.08	--
8664	1.04	--
8675	--	1.16
8683	--	1.21
8658	--	1.07
8652	--	1.19

MEAN	1.10	1.16
SD	0.059	0.062
N	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY
OF WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: M:E RATIO

STUDY ID: 193
STUDY NO: 193ME
ABBR: M:E RATIO

SEX: FEMALE

UNITS: -

Animal ID Week 14 Week 27

GROUP: 1-F:0 mg base/kg/day

8721	1.27	--
8712	1.15	--
8710	1.24	--
8723	1.25	--
8705	--	1.23
8700	--	1.31
8699	--	1.29
8690	--	1.18
MEAN	1.23	1.25
SD	0.053	0.059
N	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY
OF WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: M:E RATIO

STUDY ID: 193
STUDY NO: 193ME
ABBR: M:E RATIO

SEX: FEMALE

UNITS: -

Animal ID Week 14 Week 27

GROUP: 2-F:0.1 mg base/kg/day

8717	1.31	--
8703	1.24	--
8713	1.20	--
8693	1.16	--
8695	--	1.27
8709	--	1.26
8715	--	1.34
8697	--	1.17

MEAN	1.23	1.26
SD	0.064	0.070
N	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY
OF WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: M:E RATIO

STUDY ID: 193
STUDY NO: 193ME
ABBR: M:E RATIO

SEX: FEMALE

UNITS: -

Animal ID Week 14 Week 27

GROUP: 3-F:0.3 mg base/kg/day

8692	1.06	--
8718	1.17	--
8706	1.19	--
8714	1.22	--
8701	--	1.33
8702	--	1.24
8720	--	1.19
8704	--	1.36

MEAN	1.16	1.28
SD	0.070	0.079
N	4	4

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY
OF WR242511 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: M:E RATIO

STUDY ID: 193
STUDY NO: 193ME
ABBR: M:E RATIO

SEX: FEMALE

UNITS: -

Animal ID Week 14 Week 27

GROUP: 4-F:1.0 mg base/kg/day

8696	1.02	--
8719	1.10	--
8711	1.07	--
8716	1.13	--
8725	--	1.25
8707	--	1.35
8689	--	1.21
8722	--	1.17

MEAN	1.08	1.25
SD	0.047	0.077
N	4	4

(--) - Data Unavailable

IV. Quality Assurance Statement



Bone Marrow Evaluation Report

Thirteen Week Oral Toxicity Study of WR242511 with a Thirteen Week Recovery Period in Dogs

TRL Study Number: 193

QUALITY ASSURANCE STATEMENT

This bone marrow evaluation project has been inspected and audited by the PAI Quality Assurance Unit (QAU) as required by the Good Laboratory Practice (GLP) regulations promulgated by the U.S. Food and Drug Administration or the U.S. Environmental Protection Agency. The bone marrow evaluation report is an accurate reflection of the recorded data. The following table is a record of the inspections/audits performed and reported by the QAU.

<u>Date of Inspection</u>	<u>Phase Inspected</u>	<u>Date Findings Reported to Management/ Study Pathologist</u>
04/12/96	Individual Animal Data	04/12/96
04/12/96	Draft Bone Marrow Evaluation Report	04/12/96
04/30/96	Second Draft Bone Marrow Evaluation Report	04/30/96
05/17/96	Third Draft Bone Marrow Evaluation Report	05/17/96

Sharon E. Abel
Quality Assurance Auditor

May 17, 1996

Date

DRAFT

APPENDIX M

Protocol and Protocol Amendments

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

1.0 PURPOSE OF THE STUDY:

The purpose of this study is to determine specific target organ toxicity, dose-response relationships, and a no adverse effect level of WR242511 tartrate in Beagle dogs following thirteen weeks of daily oral administration. In addition, the reversibility of these toxic effects over a 90-day recovery period will be assessed. This study will be conducted in accordance with the specifications of the Sponsor as described in Task Order UIC-18. The protocol for this study was approved by the UIC Animal Care Committee (Appendix 1).

2.0 SPONSOR:

- 2.1 Name: U.S. Army Medical Materiel
Development Activity
- 2.2 Address: Fort Detrick
Frederick, MD 21702-5009
- 2.3 Representative: George J. Schieferstein, Ph.D.

3.0 TESTING FACILITY:

- 3.1 Name: Toxicology Research Laboratory (TRL)
- 3.2 Address: University of Illinois at Chicago (UIC)
Department of Pharmacology
1940 W. Taylor St.
Chicago, IL 60612-7353
- 3.3 Study Director: Barry S. Levine, D.Sc., D.A.B.T.

4.0 DATES:

- 4.1 Proposed Initiation of Dosing: 09/06/95
- 4.2 Proposed Necropsy Dates: 12/06 - 07/95
03/06 - 07/96 (recovery animals)
- 4.3 Proposed Study Completion Date
(Draft Study Report): 06/07/96

5.0 TEST ARTICLE

- 5.1 Name or Code No: WR242511 Tartrate
8-[(4-Amino-1-methylbutyl)amino]5-(1-hexyloxy)-
6-methoxy-4-methylquinoline DL tartrate
Base mole fraction = 0.71
Bottle No. BM05816
- 5.2 TRL Chemical No: 1720614
- 5.3 Physical Description: Yellow powder.
- 5.4 Stability and Handling of Test Article:
- 5.4.1 Storage Conditions to Maintain Stability:
- 5.4.1.1 Temperature: -20 to -15°C.
- 5.4.1.2 Humidity: Ambient conditions at -20 to -15°C.
- 5.4.1.3 Light: Protect from light.
- 5.4.1.4 Special Requirements: None
- 5.4.2 Special Handling Procedures: Standard safety precautions including gloves, eye protection, mask, and lab coats.
- 5.4.3 Log of Test Article: The amount, date, identity of person(s) removing aliquots and the purpose for which each aliquot of the test article was removed from the batch will be documented. At termination of the study, all unused test article will be returned to the Sponsor.

6.0 PERSONNEL:

Principal Investigator	Barry S. Levine, D.Sc., D.A.B.T.
Study Director	Barry S. Levine, D.Sc., D.A.B.T.
Pathologist	Robert L. Morrissey, D.V.M., Ph.D., D.A.C.V.P.
Pathology Support	Ralph M. Bunte, D.V.M., D.A.C.V.P.
Analytical Chemist	Adam Negrusz, Ph.D.
Clinical Veterinarian	Terry Hewett, D.V.M., D.A.C.L.A.M.
Veterinarian Support	Documented in raw data
Ophthalmologist	Samuel J. Vainisi D.V.M., D.A.V.C.O.
Cardiologist	Robert Hamlin, D.V.M., Ph.D., D.A.V.C.P.
Tox. Lab Supervisor	Soudabeh Soura, B.S.
Lead Technician	Teresa O'Neill, B.S.
Clinical Laboratory	Maria Lang, A.H.T., C.V.T.
Chemistry Specialist	Thomas Tolhurst, B.S.
Quality Assurance	Ronald C. Schoenbeck

7.0 TEST SYSTEM:

- 7.1 Species: Dog
- 7.2 Strain: Beagle
- 7.3 Sex(s)/Number: 32 Males & 32 Females
- 7.4 Age of Animals: Approximately 7 - 8 months old upon initiation of treatment.
- 7.5 Weight of Animals: Approximately 10 - 13 kg (males) and \approx 8 - 11 kg (females) upon initiation of treatment.
- 7.6 Source of Animals: Marshall Farms, North Rose, NY.
- 7.7 Justification for Selection of Test System: The FDA requires the use of two animal species, one being a non-rodent, in preclinical toxicology studies. The dog is a standard and accepted non-rodent species for regulatory toxicology studies, and is specified by the Sponsor.
- 7.8 Procedure for Unique Identification of Test System: Upon arrival each animal will be given a facility unique number. This number will be coded on a subcutaneously implanted microchip and will also appear on a cage card visible on the front of each run. The cage card will additionally contain the study number, test article identification, treatment group number, sex and dose level. Cage cards will be color-coded as a function of treatment group. Raw data records and specimens will also be identified by the unique test animal number.
- 7.9 Housing: The animals will be housed in an AAALAC-accredited facility in a temperature (65 - 84°F) and humidity (30 - 70%) controlled room with a 12 hour light/12 hour dark cycle. Animals may be housed two per run within sex during the quarantine/pre-test period, but will be housed singly prior to dosing initiation for the duration of the study. The run size, 15 feet², is adequate to house dogs at the upper weight range as described in the *Guide for the Care and Use of Laboratory Animals*, DHHS (NIH) No. 86.23. All runs will be cleaned and fresh bedding replaced daily. The runs will be sanitized once every two weeks.
- 7.10 Quarantine Procedure: Animals will be quarantined for approximately three weeks. During that time, the animals will be observed daily for signs of illness and all unusual observations will be reported to the Study Director or Clinical Veterinarian. Body weights and physical examinations will be done upon the dogs' arrival at the animal facility. Additionally, each dog will be lightly sprayed upon arrival with Para Pyrethrin Mist for fleas, lice, and ticks. Within approximately one week of arrival, hematology and clinical chemistry tests, and fecal examination for internal parasites will be performed. If parasites other than coccidia are found, the affected animal will be treated with a vermifuge approved by the Sponsor, and at least 10 days and a negative fecal examination will elapse before the animal is used on a study. Animals which demonstrate coccidia in their fecal samples will only be treated in a similar manner as above if they concurrently

exhibit diarrhea. All dogs will have been vaccinated against canine distemper, infectious canine hepatitis, leptospirosis, parainfluenza, parvo, oral papilloma, and rabies by the animal supplier. Animals will be examined during quarantine and approved for use by the Clinical Veterinarian prior to being placed on test. Any sickly animal will be eliminated from the animal selection process. If a selected animal appears sickly prior to initiation of treatment, it will be replaced by a healthy animal prior to treatment under the direction of the Study Director. Quarantine release will be documented by the veterinarian prior to study initiation.

- 7.11 Food: Certified Canine Diet No. 5007 (PMI Feeds Inc., St. Louis, MO), approximately 400 g, will be provided daily from arrival until termination. Exactly 400 g will be provided when food consumption is measured. The food will be removed for an overnight fast ($\approx 16 - 20$ hours) prior to blood collection, overnight urine collection or scheduled sacrifice.
- 7.12 Water: Tap water from an automatic watering system in which the room distribution lines are flushed daily will be provided *ad libitum* from arrival until termination. The water is not treated with additional chlorine or HCl.
- 7.13 There are no known contaminants in the feed or water which are expected to influence the study. The results of bi-monthly comprehensive chemical analyses of Chicago water performed by the City of Chicago are documented in files maintained by Quality Assurance.
- 7.14 It is not known if the animals will experience pain or distress during the study. Analgesic or anesthetic agents will confound the ability to determine the toxic potential of the test article, and therefore will not be used. If an animal is in severe pain or distress, following consultation with the veterinary staff, it will be euthanized in accordance with standard operating procedures.

8.0 EXPERIMENTAL DESIGN:

8.1 Treatment Groups:

<u>Treatment Group</u>	<u>Dose Level (mg base/kg/dav)</u>	<u>Number of Males</u>	<u>Number of Females</u>
1	0	4 + 4*	4 + 4*
2	0.1	4 + 4*	4 + 4*
3	0.3	4 + 4*	4 + 4*
4	1.0	4 + 4*	4 + 4*

*Recovery Animals

Thirty seven dogs of each sex will be purchased for the study. All animals not assigned to the study at the initiation of the dosing period will become the property and responsibility of UIC.

Dose levels were selected in consultation with the Sponsor based upon the results of an earlier four week oral toxicity study in the dog (UIC/TRL Study No. 134). The number of animals, 4 sex/dose, is routinely used in regulatory studies, and also is the number of animals for this species indicated in the 1993 "OECD Guidelines for the Testing of Chemicals; Subchronic Oral Toxicity - Non-rodent: 90-day Study." No such FDA document exists for the testing of drugs.

Four animals/sex/group will be necropsied in week 14. The remaining animals will be held for a thirteen week recovery period, at which time they will be necropsied.

- 8.2 Frequency and Route of Administration of the Test Article: The test article will be administered once daily by gelatin capsule starting with day 1 for at least 13 weeks. All animals will receive empty gelatin capsules for at least the last 3 days during week -1 to acclimate them to the procedure. The specific quantity of the test article (weighed to the nearest 0.1 mg) will be adjusted for purity and the base mole fraction, and will be based on each animal's most recent body weight (twice weekly in weeks 1 - 4 and weekly thereafter at the discretion of the Study Director). Control animals will receive empty gelatin capsules. The animals to be sacrificed after the 13 week treatment period will be dosed up to and including the day prior to scheduled necropsy on days 92 and 93, i.e., dosing will be for 91 or 92 days. The recovery animals will be dosed for 91 days.
- 8.3 Justification of Route(s): Oral treatment is the intended clinical route and is specified by the Sponsor.
- 8.4 Procedure to Control Bias during the Assignment of Animals to Treatment Groups: The animals will be randomized using a restricted randomization procedure, stratified by body weight, during the quarantine/pretest period. Baseline data including clinical pathology, ECG and ophthalmology data will be used to select appropriate animals for randomization.
- 8.5 Test Article Vehicle: Gelatin capsules (size 000; capacity 1.37 ml).
- 8.6 Test Article Dosage Form Preparation and Analyses: Not applicable. The test article will be given in gelatin capsules. The specific quantity in each capsule will be adjusted for purity and the base mole fraction, and will be based on each animal's most recent body weight. The neat drug will be identified by GC-MS, and will be analyzed for purity prior to and after completion of the 13 week dosing period.
- 8.7 Type and Frequency of Observations, Tests, Analyses and Measurements:
- 8.7.1 Clinical Signs: All animals will be observed once daily for clinical signs of toxicity approximately 1 - 2 hours after dosing. Additionally, all animals will be observed for moribundity/mortality in the afternoon and immediately prior to dosing in the morning. During the recovery period, clinical signs will be recorded once daily in the morning.

- 8.7.2 Clinical Observations: All animals will be subjected to a physical examination including examination of eyes and all orifices in week -2/-1, on day 0, and weekly thereafter.
- 8.7.3 Body Weight: Body weights of all animals will be recorded at test animal selection in the quarantine/pretest period, twice weekly during the first four study weeks, weekly thereafter (at the discretion of the Study Director) during the remainder of treatment and during the recovery period, and at scheduled necropsy.
- 8.7.4 Food Consumption: Food consumption for all animals will be measured over an approximate 24 hour period twice during the quarantine/pretest period, and weekly during the treatment and recovery periods.
- 8.7.5 Ophthalmologic Examinations: All dogs will be examined by indirect ophthalmoscopy prior to study initiation and during week 13, and in week 26 for the recovery animals.
- 8.7.6 Electrocardiographic Examinations: Recordings from leads I, II, III, aV_R, aV_L, and aV_F will be collected with the animal in right lateral recumbency during the quarantine/pretest period and in week 13, and in week 26 for the recovery animals. Analysis will include heart rate and duration of the P wave and PR, QRS and QT intervals.
- 8.7.7 Clinical Pathology: Hematology and clinical chemistry parameters will be measured within one week of arrival (week -3), and in weeks -1, 4, 8, and 13. Hematology and clinical chemistry tests will also be performed for the recovery animals in weeks 18 and week 26. The overnight fasted animals will be unanesthetized and sufficient blood will be collected from the jugular vein to measure the following parameters in random order. Water will be available *ad libitum* during all fasting periods.

Hematology

Activated partial thromboplastin time	Mean corpuscular hemoglobin (MCH)
Erythrocyte count	Mean corpuscular hemoglobin concentration (MCHC)
^a Erythrocyte morphology	Mean corpuscular volume (MCV)
Heinz bodies	^b Methemoglobin
Hematocrit	Platelet count
Hemoglobin	Prothrombin time
Leukocyte count, total and differential	Reticulocyte count

^aIncludes nucleated RBCs.

^bTo be measured with a Co-oximeter (Instrumentation Laboratory Model

No. 482). The assay will be performed within one hour of sample collection. The specimens will be kept on wet ice prior to analysis.

Clinical Chemistry

Alanine aminotransferase (ALT)	Globulin (calculated)
Albumin	Glucose
Albumin/globulin ratio (calculated)	Haptoglobin
Alkaline phosphatase	Lactate dehydrogenase (LDH)
Aspartate aminotransferase (AST)	Phosphorus (inorganic)
Calcium	Potassium
Chloride	Sodium
Cholesterol	Total bilirubin
Creatinine	Total protein
Creatine kinase (CK)	Triglycerides
Gamma glutamyl transferase	Urea nitrogen (BUN)

Urinalysis parameters will be measured following an overnight fast in week -1, and in weeks 4, 8 and 13, and during the recovery period in weeks 18, and 26. During the overnight fasting period, the animals will be placed in a metabolism cage for urine collection. Water will be available *ad libitum* during all fasting periods.

Urinalysis

Qualitative	
Bilirubin	Nitrite
Glucose	pH
Ketones	Protein
Occult blood	Urobilinogen
Leukocytes	
Color	
Specific Gravity	
Microscopic examination of spun sediment	

8.7.8

Pathology: All animals which die on test or sacrificed if moribund will be necropsied. Four animals/sex/group will be sacrificed and necropsied in random order over a two consecutive day period (days 92 and 93). The remaining recovery animals will be sacrificed and necropsied in random order

at the onset of week 27, after a thirteen week recovery period. This will be accomplished by sodium pentobarbital anesthesia (i.v.; 20 - 30 mg/kg) and exsanguination. An extensive necropsy will be performed under the direction and supervision of the pathologist. Terminal body weights will be collected prior to routine sacrifice.

The necropsy procedure will be a thorough and systematic examination and dissection of the animal viscera and carcass to include the external surface, all orifices, the cranial cavity, external surface of the brain, cross section of the spinal cord, the nasal cavity and nasal turbinates, thoracic, abdominal and pelvic cavities and their viscera, and cervical tissues and organs. The following tissues and organs will be collected and fixed in 10% neutral buffered formalin (NBF), except the eyes which will be fixed in 2.5% phosphate buffered glutaraldehyde.

*Adrenal glands	Nerve (sciatic)
Aorta (thoracic)	*Ovaries
*Brain (fore-, mid, and hind-)	Pancreas
Cecum	Pituitary
Colon	Prostate
Diaphragm	Rib with Marrow
Duodenum	Salivary gland (mandibular)
Esophagus	Skin
Eyes and optic nerve	Spinal cord (cervical, thoracic)
Gallbladder	*Spleen
Gross lesions	Stomach
*Heart	*Testes
Ileum	Thymus
Jejunum	*Thyroid gland with parathyroids
*Kidneys	Tongue
*Liver (with gallbladder drained)	Tonsil
Lungs/Bronchi	Trachea
Lymph node (submandibular)	Ureter
Lymph node (mesenteric)	Urinary bladder
Mammary gland	Uterus
Muscle (skeletal)	

*Weighed at scheduled necropsy. Paired organs will be weighed as a unit.

Histopathology requirements:

All tissues collected at necropsy from all dogs in all treatment groups found dead, sacrificed either *in extremis* or at scheduled necropsy in week 14 will be embedded in paraffin, sectioned, stained with hematoxylin and eosin, and examined microscopically. Those tissues/organs for which treatment-related lesions were observed will be examined microscopically for all recovery animals (week 27).

Bone marrow (rib) smears will be prepared for all animals at their scheduled necropsy. Myeloid:erythroid (M:E) ratios will be determined for all animals necropsied in week 14. If treatment-related changes are seen, M:E ratios will be determined for all recovery animals.

- 8.8 Statistical Analyses: For each sex, Analysis of Variance tests will be conducted on body weight; ECG measurements; hematology; clinical chemistry; urine specific gravity and pH; and organ weight data. Organ weight analyses will consider weights relative to brain weight. If a significant F ratio is obtained ($p \leq 0.05$), Dunnett's t test will be used for pairwise comparisons to the control group. Food consumption data will be analyzed by the Kruskal-Wallis test ($p \leq 0.05$). If a significant effect is seen, the Mann-Whitney U test will be used for pair-wise comparisons to the control group. Frequency data such as incidence of mortality, gross necropsy observations and tissue morphology observations will be compared by Fishers Exact Test or Chi-square analyses as necessary.

All statistical analysis procedures will compare treated to control animals at each time point. Data will not be corrected for baseline values, except that body weight analysis will include absolute values, weekly changes and total weight changes. Baseline clinical pathology data will be used to assess the general health of the animals, and may be used qualitatively to assist in the interpretation of potential drug-related changes following the initiation of treatment.

- 8.9 Deliverables: Quantitative data will be tabulated and presented in the report, which will include historical control clinical pathology data. In addition to the written report, individual data tables in "ASCII" form and summary data tables of parameters and variability will be transmitted to the Sponsor on magnetic media (computer diskette). The transcribed data on disk will no longer be considered GLP compliant.

9.0 RECORDS TO BE MAINTAINED:

All data generated during the conduct of the study, except those that are generated as direct computer input, shall be recorded directly, promptly, and accurately in ink in bound books with prenumbered pages or on worksheets that shall be bound during or at the conclusion of the nonclinical laboratory study. All appropriate computer and machine output shall be bound during or at the conclusion of the study. All data entries shall be dated on the day of entry and signed or initialed by the person entering the data.

Any changes in entries for whatever reason (e.g., to correct an error or transposition) shall be made so as not to obscure the original entry. shall indicate the reason for such change, and shall be dated and signed or identified at the time of data input. In computer driven collection systems, the operator responsible for direct data input shall be identified at the time of data input. Any changes in computer entries for whatever reason (e.g., to correct an error or transposition) shall be made in such a manner so as not to obscure the original entry, if possible, shall indicate the reason for such change, and shall be dated and the responsible individual shall be identified. All recorded data shall be reviewed, signed and dated by a knowledgeable person, other than the person making the entry, to assure adherence to procedures and to verify observations.

Upon completion of the study and submission of the final report, all raw data, documentation, specimens, test article reserves and other materials necessary to reconstruct the study will be stored in the TRL archives maintained by Quality Assurance.

All changes or revisions, and reasons therefore, to this protocol once it is approved shall be documented, signed by the Study Director and Sponsor, dated and maintained with the protocol.

10.0 REGULATORY REQUIREMENTS:

This study will be performed in compliance with the UIC/TRL Quality Assurance Program designed to conform with FDA Good Laboratory Practice Regulations and EPA Good Laboratory Practice Standards.

Will this study be submitted to a regulatory agency? Yes If so, to which agency(ies)? Food and Drug Administration

Does the Sponsor Request that test article samples be returned? Possibly; direction to be provided by the Sponsor.

Does the Sponsor request that samples of the test article/carrier mixture(s) be returned to the Sponsor? Not applicable

11.0 PROTOCOL APPROVAL:

STUDY DIRECTOR:

Clyde W. Wheeler
Clyde W. Wheeler, Ph.D.

7/3/95
Date

PRINCIPAL INVESTIGATOR:

Barry S. Levine
Barry S. Levine, D.Sc., D.A.B.T.

7/3/95
Date

QUALITY ASSURANCE:

Ronald Schoenbeck
Ronald Schoenbeck

7/5/95
Date

SPONSOR APPROVAL:

George J. Schieferstein
George J. Schieferstein, Ph.D.
Contracting Officer's
Representative (COR)

7/10/95
Date

COMMENTS FROM THE COR:

Office of the Vice Chancellor for Research (M/C 672)
310 Administrative Office Building
1737 West Polk Street
Chicago, Illinois 60612-7227
(312) 996-4995

Contract No.: DAMD17-92-C-2001
Task Order No.: UIC-18A
Study No.: 193

APPENDIX 1

June 27, 1995

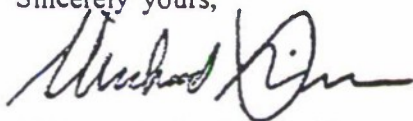
Barry S. Levine
Med - Pharmacology
312 BGRC, M/C 868

Dear Dr. Levine:

The modifications requested in your correspondence of June 23, 1995 pertaining to your approved protocol ACC: #93-033-20: "Thirteen Week Oral Toxicity Study of WR242511 With A Thirteen Week Recovery Period in Dogs" have been reviewed in accordance with the Animal Care and Use Policies of the University of Illinois at Chicago. You will be pleased to know that the modifications were approved on June 27, 1995 and consequently the records of Animal Care Committee will be revised to reflect these changes.

Thank you for complying with the Animal Care Policies and Procedures of UIC.

Sincerely yours,



Michael W. Levine, Ph.D.
Chair, Animal Care Committee

MWL:st
xc: BRL

PROTOCOL AMENDMENT

Study No.: 193

Title: Thirteen Week Oral Toxicity Study of WR242511 With a Thirteen Week Recovery Period in Dogs

1. Page 1 Section 4.0

Add the study dates as follows:

- | | | |
|-----|---|---|
| 4.1 | <u>Proposed Initiation of Dosing:</u> | 09/06/95 |
| 4.2 | <u>Proposed Necropsy Dates:</u> | 12/06 - 07/95
03/06 - 07/96 (recovery animals) |
| 4.3 | <u>Proposed Study Completion Date</u>
<u>(Draft Study Report):</u> | 06/07/96 |

Reason: The study dates have been finalized.

2. Page 2 Section 6.0

Indicate Teresa O'Neill as the Lead Technician.

Reason: Clarification of the study personnel.

3. Page 3 Section 7.5

Change the approximate body weight range to "≈ 10 - 13 kg (males) and ≈ 8 - 11 kg (females)" from "≈ 10 - 12 kg (males) and ≈ 8 - 10 kg (females)".

Reason: Clarification of the protocol.

4. Page 4 Section 7.11

In the last sentence, indicate that food will also be removed for an overnight fast (≈ 16 - 20 hours) prior to "overnight urine collection".

Reason: Clarification of the protocol.

5. Page 5 Section 8.2

- A. Indicate that dosing initiation will start on "day 1" instead of on "day 0".
- B. Indicate that animals sacrificed after the 13 week treatment period will be dosed up to and including the day prior to scheduled necropsy on "days 92 and 93" instead of "days 91 and 92", i.e. dosing will be for 91 or 92 days.

PROTOCOL AMENDMENT

Study No.: 193

Title: Thirteen Week Oral Toxicity Study of WR242511 With a Thirteen Week Recovery Period in Dogs

5. contd.

Reason: Day 1 is now defined as the first day of dosing and therefore, the scheduled necropsy days are shifted by one day.

6. Page 7 Section 8.7.8

Remove the requirement of the collection of blood for plasma drug level analysis from the protocol.

Reason: Because an analytical method for the analysis of WR242511 in dog plasma was not established by Dr. Lin (UCSF) prior to the initiation of treatment, the Sponsor has indicated that this task is no longer a protocol requirement.

7. Page 7 Section 8.7.9

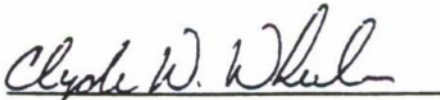
A. Renumber the "Pathology" section to "Section 8.7.8" from "Section 8.7.9".

B. In the second sentence, indicate that four animals/sex/group will be sacrificed and necropsied in random order over a two consecutive day period "(days 92 and 93)" instead of "(days 91 and 92)".

Reason: A. Following the removal of the "Plasma Drug Levels" section, the "Pathology" section sequentially becomes "Section 8.7.8". B. Because dosing initiation is now defined as day 1 instead of day 0, the scheduled necropsy days are shifted by one day.


Approvals:

STUDY DIRECTOR:


Clyde W. Wheeler, Ph.D.

8/30/95
Date

SPONSOR APPROVAL:


George J. Schieferstein, Ph.D.
Contracting Officer's
Representative (COR)

9/7/95
Date

PROTOCOL AMENDMENT

Study No.: 193

Title: Thirteen Week Oral Toxicity Study of WR242511 With a Thirteen Week Recovery Period in Dogs

8. Page 1 Section 3.3

Change the Study Director from "Clyde W. Wheeler, Ph.D." to "Barry S. Levine, D.Sc., D.A.B.T.".

Reason: Dr. Wheeler has resigned from UIC.

9. Page 2 Section 6.0

Change the Study Director from "Clyde W. Wheeler, Ph.D." to "Barry S. Levine, D.Sc., D.A.B.T.".

Reason: Dr. Wheeler has resigned from UIC.

10. Page 8 Section 8.7.8

Indicate in the second paragraph, that the eyes will be fixed in 2.5% phosphate buffered glutaraldehyde.

Reason: Change requested by pathologist to ensure proper fixation of the dogs' eyes.

11. Page 10 Section 11.0

Indicate that "Barry S. Levine, D.Sc., D.A.B.T." is the Study Director.

Reason: Clarification of the study personnel.


Approvals:

FORMER STUDY DIRECTOR:


Clyde W. Wheeler, Ph.D.

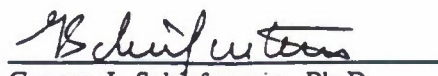
10/6/95
Date

CURRENT STUDY DIRECTOR:


Barry S. Levine, D.Sc., D.A.B.T.

10/6/95
Date

SPONSOR APPROVAL:


George J. Schieferstein, Ph.D.
Contracting Officer's
Representative (COR)

10/10/95
Date

PROTOCOL AMENDMENT

Study No.: 193

Title: Thirteen Week Oral Toxicity Study of WR242511 With a Thirteen Week Recovery Period
in Dogs

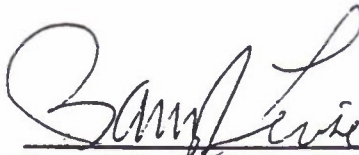
12. Page 8 Section 8.7.8

Remove the asterisk from the uterus.

Reason: Mistake in protocol.

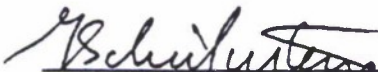
Approvals:

STUDY DIRECTOR:


Barry S. Levine, D.Sc., D.A.B.T.

1/16/96
Date

SPONSOR APPROVAL:


George J. Schieferstein, Ph.D.
Contracting Officer's
Representative (COR)

1/16/96
Date

APPENDIX N
Study Deviations

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR238605 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN DOGS

Study Deviations*

<u>Deviation Type</u>	<u>Specific Deviation</u>	<u>Effect on Study</u>
Protocol	The humidity was out of range at various times during the in-life phase of the study. The humidity never went below 22% (the acceptable range was 30 - 70%).	None. The deviations were minimal.

* The detailed "Deviation Reports" are contained in the raw data which are archive at the Toxicology Research Laboratory, University of Illinois at Chicago, Department of Pharmacology, 1940 W. Taylor St., Chicago, IL 60612

The above deviations did not affect the integrity of the study.

Barry S. Levine, D.Sc., D.A.B.T.

Date